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EARLY AMBULATION FOLLOWING SECTION OF THE ANTERIOR ABDOMINAL WALL

AN ANALYSIS OF FOUR HUNDRED AND TWENTY-SIX PERSONALLY CONDUCTED CASES

HARRY NELSON, M.D.

NEW ORLEANS

Some years ago, on the basis of two more or less accidental observations, I began to question whether the time-honored practice of absolute rest in bed following an abdominal section was really in the best interests of the patient. The first observation concerned the excellent healing of wounds and the low incidence of postoperative complications in children, in spite of the fact that they are never restrained after operation and that their movements, from the moment of their recovery from anesthesia, sometimes approach violence. The second had to do with the similarly excellent healing of wounds in animals submitted to abdominal section for various experimental procedures; in most instances complications of the wounds were notably absent, and I have observed and, on inquiry, could learn of no instance of disruption of a wound under these circumstances.

As the result of these observations I undertook a review of the literature dealing with early rising after operation, while at the same time I proceeded to put the plan into cautious practice in my personal cases. I am now able to report a series of 429 operations through 426 incisions of the anterior abdominal wall in 423 patients, for whom, as will be pointed out, the incidence of postoperative complications was considerably lower than might be expected in a similar series in which the subjects were not ambulated, while at the same time no harm accrued to the patients, whose convalescence was actually smoother and more rapid than that under the old practice of prolonged rest in bed.

REVIEW OF THE LITERATURE

The literature of early postoperative walking was extensively reviewed by Newburger[1] in 1943, and repetition of his long bibliography would not be justified here. A few of the more important communications, however, must be mentioned.

Ries,[2] in 1899, seems to have been the first to state that "the period for which it was advisable to confine such cases [surgical patients] to bed could be counted by hours instead of days." His temerity was originally limited to patients who had undergone "vaginal celiotomy" but was soon extended to patients who had been subjected to "ventral celiotomy," the rationale being that since it is impossible to keep other parts of the body, such as the tongue, the chest or the veins, at absolute rest after a surgical operation, there is no reason why the abdominal wall should be kept at rest either. He declared himself thoroughly satisfied with the results of early ambulation, which included a striking absence of ileus and of loss of muscle tone, as well as improvement in the happiness of the patient; however, he supplied no statistics.

In the foreign literature (cited by Newburger), the discussion seems to have been opened by Rehn, in 1902, with the statement that immobilization after operation, regardless of its possible desirability from the standpoint of the healing of the wound, is detrimental to the patient as a unit. This consideration was the basis for Henle's "promenade in bed" (*Spaziergang im Bett*), which was not, however, reported until 1908, in which year Kümmell recommended the practice of early rising after operation.

Boldt,[3] in 1907, supplemented an apparently informal report on the subject two years earlier with a statistical study of 384 personal cases, including cases in which "complicated" operations on the intestinal tract were done. Many of the patients had been permitted out of bed within twelve hours after operation. The only complications in the series were 2 instances of mild

From the Independent Surgical Service of Charity Hospital of Louisiana at New Orleans.

1. Newburger, B.: Early Postoperative Walking: II. Collective Review, Surgery **14**:142-154 (July) 1943.

2. Ries, E.: Some Radical Changes in the After-Treatment of Celiotomy Cases, J. A. M. A. **33**:454-456 (Aug. 19) 1899.

3. Boldt, H. J.: The Management of Laparotomy Patients and Their Modified After Treatment, New York M. J. **85**:145-153 (Jan. 26) 1907.

phlebitis of the lesser saphenous vein, although during the period of observation there had been 4 instances of postoperative thrombosis in other patients who for various reasons had been kept in bed. Boldt found many advantages and no disadvantages inherent in the plan in properly selected cases.

In the same communication Boldt commented on the "more than 500" abdominal sections reported to him by Ries in November 1906, after which the only complication had been a single infected wound in an incisional hernia. He also stated that, including his own and Ries's series, he then had knowledge of more than 1,000 patients who had been treated by early postoperative ambulation, without serious consequences in any and with generally good results in all but a few scattered instances.

Following Boldt's report, numerous articles on the subject of early postoperative ambulation appeared in the continental literature, some of them dealing with many hundreds of cases and all of them reporting uniformly good results. In many of these reports, however, "early" meant seventy-two hours or more after operation, and large numbers of the operations were not intraperitoneal procedures.

The American literature was practically devoid of articles on the subject from Boldt's communication in 1907 until 1941, when Leithauser and Bergo [4] published a report of 436 surgical operations, which included, in addition to 370 appendectomies, 18 cholecystectomies, 2 splenectomies and 1 gastrectomy. Dehiscence of the wounds, pneumonitis, thrombophlebitis and other serious complications were notably lacking except for a single instance of continued hemorrhage following gastrojejunostomy for a peptic ulcer. In 1943 Leithauser [5] increased the number of operations in the series to 900, by the addition of 274 appendectomies and 190 other major surgical procedures, including 25 cholecystectomies and 3 gastrectomies. Both series, however, included operations which did not involve opening of the peritoneal cavity, and in neither report are details supplied as to the number and the duration of follow-up observations.

Untoward results in the combined series included: 2 deaths after partial gastrectomy (1 patient with carcinoma of the stomach died of a subhepatic abscess, and the other, who had a perforated peptic ulcer, died of hepatitis and inanition); 4 infections of wounds, which occurred respectively after appendectomy and after femoral, inguinal and incisional hernioplasty (nylon sutures had been used for the incisional and the inguinal hernioplasties); 5 instances (7 per cent) of recurrent hernia; 1 instance each of separation of the wound and of thrombophlebitis; 3 readmissions to the hospital, 1 for thrombophlebitis following cholecystectomy and 2, following appendectomy, for a cul-de-sac abscess and for peritonitis respectively.

In 1942 Nelson and Collins [6] reported a series of 115 gynecologic operations (exclusive of 33 operations in which the anterior abdominal wall was not incised) after most of which the patients were ambulated within twenty-four hours. These authors carried out the plan on the principles which we follow and which will be stated later. They reported rapid convalescence, early return of normal function of the bladder and the bowel and complete absence of postoperative complications except for infections of wounds, the usual incidence of which, however, was greatly reduced.

It is only fair, in analyzing the literature, to remember that both the first American and the first European advocates of early postoperative ambulation were handicapped by the limitations of the surgical era in which they practiced. Their physiologic knowledge was imperfect; their suture material was poor as compared with material used at the present time, and the protein and vitamin concentrates now available to insure optimum healing of wounds were completely lacking to them.

CRITERIA OF EARLY POSTOPERATIVE AMBULATION

Some definition of terms is necessary before proceeding to an analysis of this series of operations. In my practice the term "early," which is variably used in other reports, always represents the seventy-two hour period immediately following operation. This limitation automatically excludes from this report a large number of operations on patients who were ambulated after this time, though still well before the time at which patients are usually permitted out of bed. My colleagues and I feel that the seventy-two hour period should be emphasized, because the majority of pulmonary complications, which constitute the most important group of postoperative

4. Leithauser, D. J., and Bergo, H. L.: Early Rising and Ambulatory Activity After Operation: A Means of Preventing Complications, Arch. Surg. **42:** 1086-1093 (June) 1941.

5. Leithauser, D. J.: Confinement to Bed for Only Twenty-Four Hours After Operation: A Means of Preventing Pulmonary and Circulatory Complications and of Shortening the Period of Convalescence, Arch. Surg. **47:**203-215 (Aug.) 1943.

6. Nelson, E. W., and Collins, C. G.: Cotton Suture Material and Early Ambulation in Gynecology and Obstetrics, Am. J. Obst. & Gynec. **12:**109-114 (July) 1942.

complications, develop well within this limit. For many reasons we do not advocate permitting patients to walk from the operating room after abdominal section, as advised by certain Continental writers.

No patient is forced to practice early rising who is unwilling to attempt it. We merely present our recommendations, supported by results, to eligible patients and permit them to get up or remain in bed, as they choose. Surprisingly few refuse early ambulation. Sometimes, even before the plan is presented to them, patients request permission to attempt it because they have observed good results in their associates in the ward. Some who at first refuse to leave their beds later do so when they observe the smoothness of convalescence in those who practice the plan.

Early ambulation is not carried out in the presence of any of the following contraindications:

1. Failure to observe any of the prerequisites of optimum healing of wound, including failure to carry out the tenets of Halsted as to the closure of a wound, the use of suture materials other than wire or cotton and the existence of deficiencies of vitamins and hypoproteinemia.

2. Conditions for which absolute rest in bed is demanded, such as shock peritonitis, active hemorrhage, cardiac failure, pneumonitis and impending or actual thyroid crisis.

3. Potential or actual complications of the wound, including gross contamination, infection, hemorrhage and dehiscence.

4. Pregnancy in which abortion is feared. Pregnancy per se is not a contraindication.

5. Extreme debility, for which ambulation is deferred until there is some restoration of strength and muscle tone, as a result of sitting up.

6. Second stage of a thoracolumbar sympathectomy, after which the patient, because of sudden alterations in the vascular system, cannot immediately tolerate the upright position.

7. Lack of adequate and intelligent nursing supervision. It is true that in one sense early ambulation reduces the amount of nursing care necessary. On the other hand, it is important that the nursing supervision be adequate to insure that the patient obeys instructions as to when and how long he shall walk.

In my opinion only cotton and wire are suitable for use in these circumstances, because they alone combine most of the desiderata of ideal suture material. Although others have employed catgut in operations after which early ambulation was practiced, its use is associated with a high degree of irritability of tissues and a high incidence of contamination of wounds and, like nylon, it does not have the ability to retain square knots consistently. Wounds closed with it, as well as those closed with silk, become dangerously weak on the third and fourth days respectively, as pointed out by Localio and his associates[7] (chart) and do not approximate even the minimum strength of wounds closed with cotton until the fifth postoperative day. Nylon, while approaching cotton in its ability to maintain tensile strength in the wounds during the lag period, may, as pointed out by Leithauser, be responsible for the development of granulomas as late as ten months after operation. On the other hand, cotton causes minimal irritability of tissues, is associated with a minimal incidence of contamination of wounds and holds square knots reliably, and the tensile strength of a wound sutured with it (chart) at no time drops below 75 per cent of the strength of the intact abdominal wall.

OUTLINE OF PLAN OF EARLY AMBULATION

As soon as the patient has fully recovered from the effects of anesthesia (in my opinion the particular anesthetic agent used is not significant), the bed is sharply tilted, so that the head is elevated. After this position has been maintained for a time, the bed is leveled and the patient assumes a sitting position on the side of the bed, with the feet resting on a chair. In this position he breathes deeply and coughs frequently. He then lies down, and the head of the bed is again sharply elevated. After a second period of rest he is assisted to stand and is conducted to the bathroom, where the bladder is practically always emptied without difficulty. If his condition is good, and if he wishes, he sits up in a chair for a time before returning to bed. The rapidity with which these different steps are carried out varies with the individual case, but ordinarily there is no great delay between them.

After the pain of the initial ambulation patients seldom complain again of even significant discomfort. Those who are oversensitive to the pain of the first rising or who are unduly apprehensive are made to practice sitting at the edge of the bed, with intervals of rest between each attempt, until they are strong enough and willing to walk to the bathroom. After the initial ambulation all patients are allowed to rise as often as they please, to go to the bathroom, which they invariably prefer to the use of the bedpan, to fetch drinks and to sit on the sun porch.

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7. Localio, S. A.; Casale, W., and Hinton, J. W.: Wound Healing—Experimental and Statistical Study: IV. Results, Surg., Gynec. & Obst. **77**:376-388 (Oct.) 1943.

Greatly debilitated patients may find it necessary to confine their first out of bed activities to the use of a wheel chair and a commode, but even these persons exhibit a more rapid return of strength than do other patients in the ward who, although perhaps originally stronger, lose strength by continued confinement to bed. It is important, however, that the initial activities of all patients be supervised by the nursing staff and that excessive fatigue be prevented by frequent intervals of rest in bed, for many, in their enthusiasm, are inclined to overdo. It should also be emphasized that periodic breathing exercises and coughing are part of the regimen of postoperative activity.

Although Boldt used a plaster scultetus bandage to immobilize the abdominal parietes as part of his routine and kept it in place for three or four weeks, I regard any sort of abdominal support as unnecessary and undesirable. The modern concept of postoperative pulmonary complications considers freedom of the excursion of the lower ribs as an important factor in the prevention of such complications.

Drainage does not affect the routine of early rising. Tubes in the stomach, gallbladder, intestine or bladder are merely clamped and disconnected while the patient is out of bed.

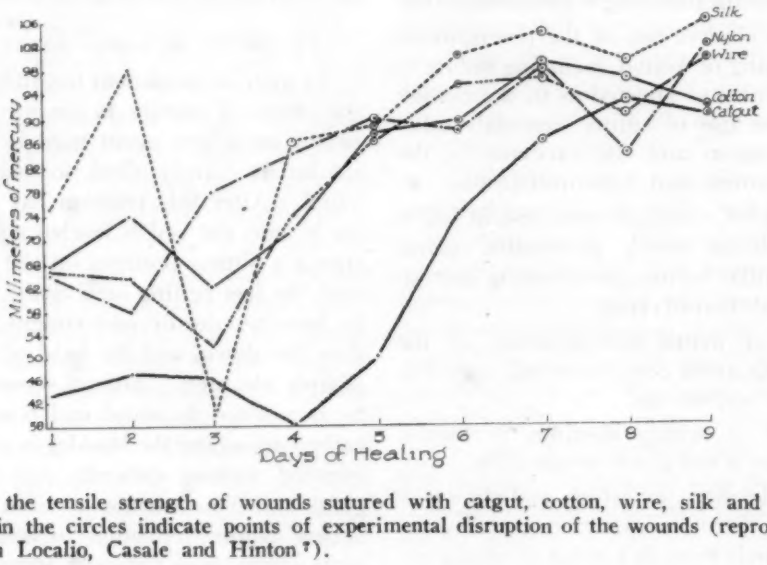


Chart showing the tensile strength of wounds sutured with catgut, cotton, wire, silk and nylon. The dots and the dots within the circles indicate points of experimental disruption of the wounds (reproduced [with slight modification] from Localio, Casale and Hinton[7]).

ANALYSIS OF A SERIES OF OPERATIONS

The series presented herewith consists of 429 operations carried out through 426 incisions of the anterior abdominal wall on 423 patients (table). This series does not include the large number of operations after which early ambulation was practiced but in which the anterior abdominal wall was not opened; it is obvious that whatever advantages accrue from the plan when the peritoneal cavity is opened will be equally valid when it is not. Many operations, furthermore, are excluded from the series because, although they were on patients who walked within seventy-two hours, that fact was not recorded and the analysis is limited to operations on patients for whom the charts were complete. For the same reason the number of operations after which the patients walked on the first day is known to be greater than the number stated; the nurse merely failed to record ambulation until the second or third day.

On the basis of the records, 258 of the patients walked within twenty-four hours, 86 walked within forty-eight hours and the remainder walked within seventy-two hours. It is worth pointing out that among those operations on patients who walked on the first day were 4 of the 5 incisional hernioplasties and most of the inguinal, femoral and umbilical hernioplasties; 3 colostomies; 2 gastrostomies, and 1 cholecystectomy and resection of an anomalous bile duct. The operations on patients who walked on the second day included 2 gastrectomies and resection of the left half of the colon, reduction of a volvulus and Lahey resection of the rectum.

While the great majority of operations in this series were on patients in late adolescent or early adult life, as would be suspected from the preponderance of appendectomies, the age range was from 18 months to 82 years. The patients submitted to hernioplasty were chiefly between 40 and 50 years of age. An 80 year old patient who had had bilateral inguinal hernias repaired asked

for permission twelve months after operation to ride a bicycle; when it had been given, he stated that he had been doing so for some time and merely desired official sanction.

The 426 abdominal incisions included 286 transverse incisions, of which 9 were high, 9 median and 268 low; 64 vertical incisions, of which 5 were high, 7 median and 52 low, and 76 oblique incisions, of which 3 were high and 73 low. The large proportion of transverse incisions in this series of operations should be noted. Tension in this type of wound is minimal, and its other advantages have recently been pointed out by Rees and Coller.[8]

Early Ambulation After Four Hundred and Twenty-Nine Intraperitoneal Surgical Procedures Through Four Hundred and Twenty-Six Incisions of the Anterior Abdominal Wall

Operation	Number of Operations
Appendectomy (for disease limited to appendix)	317
Hernioplasty	
Inguinal	59
Femoral	3
Umbilical	12
Incisional	5
Gastric operations	
Partial gastrectomy	2
Gastrostomy	2
Gastrorrhaphy	1
Intestinal operations	
Resection of left half of colon	1
Resection of terminal ileum	1
First stage Lahey resection of rectum	2
Abdominoperineal resection of rectum	2
Reduction of volvulus of sigmoid	1
Closure of colostomy	4
Operations on the biliary tract and the liver	
Cholecystectomy	3
Choledochostomy	1
Resection of anomalous bile duct	1
Hepatorrhaphy	1
Miscellaneous operations	
Exploration	4
Presacral sympathectomy	1
Repair of diastasis recti	1
Repair of diaphragm	1
Oophoropexy	1
Complete hysterectomy, bilateral salpingo-oophorectomy	2
Secondary closure of wound	1

Results.—Although the single death in this series was from cerebral thrombosis, which obviously is not related to early rising, an unfortunate series of errors occurred after this particular operation, in which a combined abdominoperineal resection was done on a 66 year old woman. The supply of sterile cotton was inadequate, and the lower half of the wound, exterior to the peritoneum, had to be closed with catgut. For this reason the usual order for early postoperative ambulation was omitted from the postoperative orders, but the resident for the ward, who had not been present at the operation, failed to note this fact and wrote a later order for the usual routine to be carried out. The confusion was discovered after the first ambulation, and the patient was thereafter kept in bed with absolute rest. Three days later, however, the catgut-closed portion of the wound separated, although the cotton-closed portion remained intact. Secondary closure was done with wire. On the fourth postoperative day the patient showed signs pointing to a cerebrovascular accident, and somewhat later signs of pulmonary congestion. Death occurred ten days after operation and four days after secondary closure. The clinical diagnosis of cerebral thrombosis and pulmonary congestion was confirmed at autopsy, which revealed the wound to be in good condition and the peritoneal cavity free from infection.

Two additional instances of partial separation of the wound occurred after operations in this series, in 1 of which, as in the case just described, early ambulation was not ordered. The patient had been submitted to incisional herniorrhaphy, for which catgut had been used. Entirely without authorization she left her bed on the second postoperative day, and three days later a small separation of the wound was observed. It was closed with wire, and convalescence thereafter was uneventful. The third case of dehiscence represented a failure on the part of the surgeon as well as on the part of the wound. The patient, a 35 year old man, had been stabbed in the abdomen and had lost a large quantity of blood. Exploration through an upper right rectus incision revealed no visceral injury. Through an inexcusable oversight no blood or plasma was administered and an order for early ambulation was written. The wound gaped slightly on the fourth postoperative day and was reapproximated with wire. At the time of writing, eighteen months after the operation, there was no evidence of hernia.

Other complications observed in the hospital included: 8 instances of infection of the wound and 1 instance of stitch abscess; 1 instance of pneumonitis, in a case of carcinoma of the esophagus, with mediastinal extension and severe bronchorrhea; 1 instance each of atelectasis, pneumonitis, edema of the scrotum, edema of the spermatic cord and abortion. The abortion was suspected to have been self induced, since the patient had made it clear that she did not wish the child, but no proof could be obtained.

It will be noted that there is a striking absence of such complications as embolism, phlebitis, peritonitis and infection of the urinary tract, a certain number of which, by the law of averages, might be expected to occur in a series of this size.

8. Rees, V. L., and Coller, F. A.: Anatomic and Clinical Study of the Transverse Abdominal Incision, Arch. Surg. **47**:136-146 (Aug.) 1943.

Of the patients reported here, 301 (71 per cent) have been observed after operation in the clinics of the Charity Hospital of Louisiana at New Orleans for periods up to two years. Most of the remainder have been heard from by letter or are known to have been accepted for full military duty in the condition in which they presented themselves. Since almost 90 per cent of all delayed postoperative complications are observed within three months after operation and most of the remaining 10 per cent within twelve months, it may be assumed that the complications observed during this two year period represent practically all that are likely to occur in these patients. They included: 2 small incisional hernias, 1 following closure of a colostomy opening, improperly executed by me, and the other in an infected lower right rectus incision, made for exploration for a stab wound (hernioplasty has been carried out in each case, but too recently to state the final results); 1 recurrent hernia, following incisional hernioplasty (repair was difficult because of the widespread destruction of the anterior rectus sheath by previous infection, and it was later determined from the operator that only the posterior rectus sheath and the superficial fascial layer had been approximated in the course of the repair); 2 painful scars, both relieved by a local injection of procaine hydrochloride, 2 infections of wounds; 2 stitch abscesses and 1 extrusion of a suture in a clean wound; 1 instance of edema of the spermatic cord and 1 instance of edema of the scrotum.

COMMENT

As this and other reports indicate, the chief benefit derived from the practice of early ambulation is the reduction of postoperative complications, for which, as Rehn (cited by Newburger) aptly stated, the bed is a veritable breeding place. Since the majority of the deaths which follow surgical operations are the result of postoperative complications, it follows that the practice of early rising can fairly be said to play a part in the reduction of postoperative mortality.

Two groups of postoperative complications, pulmonary and vascular, are particularly important. Opinions may differ as to their pathogenesis, but there is no difference of opinion as to their seriousness and as to the relative or absolute ineffectiveness of all measures which have been proposed to reduce their incidence and severity.

This is not the place to enter into a detailed discussion of the pathogenesis of postoperative atelectasis and pneumonitis, but certain pertinent facts may be stated (in greatly oversimplified form): 1. A reduction of the vital capacity of the lungs occurs after operation and may amount to 50 per cent or more. It is most frequently evident, and is evident in the maximum degree, in patients with upper abdominal incisions, for whom the period of restoration to normal vital capacity is also longest. 2. The most important factor in the production of postoperative pulmonary complications is the state of hypoventilation which occurs during anesthesia and which is likely to continue for some hours or some days thereafter. 3. The cough reflex is dulled or may temporarily cease to function after operation when the patient is in the recumbent position. As a result, bronchial secretions stagnate and dry, bronchial obstruction follows and the chain of events terminates in atelectasis and pneumonitis.

Experimental evidence is furnished by the demonstration of Kaltreider and McCann [9] as to the effectiveness of exercise in increasing both the tidal volume and the ventilation coefficient and by the demonstration of Barman and his associates [10] in corroboration of the hypothesis of Gesell, Haldane and Henderson that muscular exertion results in an alteration in the blood which clinically stimulates the respiratory centers. The remarkably low incidence of pulmonary complications in the series of operations reported herewith, as well as in the other series reported in the literature, furnishes adequate clinical evidence of the value of early rising in the prevention of these complications.

The pathogenesis of thrombosis and embolism (also stated in a greatly oversimplified form) is about as follows: Clotting is a result of chemical alterations of the blood following operation and anesthesia, combined with a deceleration of the rate of venous flow. This deceleration is a direct result of decreased muscular activity and of general loss of tone of the vascular system, as a consequence of recumbency.

Ample statistical evidence exists as to the value of early rising in the prevention of thrombosis and embolism. At the Essinger University Clinic, for instance (cited by Ochsner and DeBakey [11]), the incidence of thrombosis and fatal

9. Kaltreider, N. L., and McCann, W. S.: Respiratory Response During Exercise in Pulmonary Fibrosis and Emphysema, J. Clin. Investigation **16**:23-40 (Jan.) 1937.

10. Barman, J. M.; Consolazio, F., and Moreira, M. F.: Relation Between Pulmonary Ventilation and Oxygen Consumption After Exercise, Am. J. Physiol. **138**:16-19 (Dec.) 1942.

11. Ochsner, A., and DeBakey, M.: Therapeutic Considerations of Thrombophlebitis and Phlebothrombosis (Shattuck Lecture), New England J. Med. **225**:207-227 (Aug. 7) 1941.

embolism was 2.63 and 1.4 per cent respectively, after 1,504 operations from 1906 to 1912, in which period the patients were allowed out of bed at the end of the second week. The corresponding incidence for the 2,053 operations during the next six years, when the patients rose between the second and fifth postoperative days, was respectively 1.75 and 0.6 per cent. Von Jaschke (cited by Ochsner and DeBakey) presented similar figures: Among 300 cases in which late rising was practiced the incidence of thrombosis and fatal embolism was respectively 2 and 1 per cent, as compared with 0.5 and 0 per cent respectively among 387 cases in which early rising was practiced.

Fear that the wound will fail to heal properly is the chief objection advanced to early ambulation, and it is easy to understand why it exists, since the dependence of the healing of a wound on immobilization has been taught since ancient times. To this objection there are two possible replies: 1. Improvement in surgical technic and, in particular, improvement in suture material make a comparison with reports of even a decade ago misleading. 2. There is a complete absence or an extremely small percentage of disruptions of the wounds in the reported series of operations after which early ambulation was practiced.

Proof exists, furthermore, that early rising (unrestricted movement) after operation hastens the healing of a wound, whereas late rising (restricted movement) hinders it. In 1936 Kimbarovskiy (cited by Newburger) reported an experimental study which showed a delay in fibroplasia in dogs in which exercise was restricted after abdominal incision, and Shaus, Pozharskiy and Abrikosov agreed with this conclusion. Newburger,[12] in 1943, demonstrated that exercise rather than immobilization expedited the healing of wounds in experimental animals submitted to incision of the abdominal wall. There was a notable acceleration of the acquisition of tensile strength in the unrestricted animals, as the result of a shortening in the lag period, or, conversely, a more rapid initiation of the period of fibroplasia, as compared with the processes studied in control animals. Clinical proof as to the effect of unrestricted movement on the healing of wounds is furnished in the various reports cited throughout this communication.

The advantages of early rising observed in our own series corroborate those listed by Boldt in his report. The improvement in the patient's morale is a psychologic advantage which must not be overlooked, nor must the more rapid convalescence and the briefer period of hospitalization, which result in economic saving to both patient and hospital. The medical and nursing staffs attached to our wards have been impressed with the smooth convalescence of patients who are ambulated early and have commented particularly on the infrequent incidence of catheterization, as compared with the usual postoperative incidence.

The low incidence of postoperative complications in patients ambulated early is the obvious answer to possible charges of malpractice. The question was first raised by Boldt in 1907 and was answered by him then as satisfactorily as it could be answered today: To prove that this practice is responsible for such postoperative complications as occur (he spoke particularly of thrombosis and embolism), it would be necessary to prove that these complications do not occur in patients kept in bed for conventional periods of time.

The same author's devastating observation that those who oppose the plan of early postoperative ambulation are generally those who have had no experience with it is also still valid. Furthermore, it is fair to emphasize that poor results obtained by those who ignore the definite criteria established for early ambulation do not constitute a valid reason for condemning the whole plan.

SUMMARY AND CONCLUSIONS

Although early ambulation following intra-abdominal operations was first recommended in 1899, the practice has never been generally followed, and most of the few critically analyzed series have been published within the last two or three years.

An analysis of this series of 429 operations through 426 incisions of the anterior abdominal wall after which ambulation was practiced within seventy-two hours shows that the majority of the patients walked on the day of operation or within the first twenty-four hours.

The incidence of immediate and delayed complications in this series was minimal. Of the 3 partial disruptions of a wound 2 occurred in patients whose wounds had been closed with catgut and for whom early ambulation had not been authorized. The third was due to an error on the part of the surgeon, who failed to order transfusions of blood and plasma for a patient who had lost a large amount of blood. Only 2 incisional hernias, both small, were observed, and there was 1 instance of recurrent incisional hernia in a patient in whom repair was inadequate. The

12. Newburger, B.: Early Postoperative Walking: I. The Influence of Exercise on Wound Healing in Rats, Surgery **13**:692-695 (May) 1943.

single fatality in the series was due to cerebral thrombosis.

Good results depend on the strict observance of contraindications as well as of indications.

The advantages of the plan include the lowered incidence of postoperative complications, particularly pulmonary and vascular complications; the lower incidence of nausea, vomiting and abdominal distention; the earlier return of normal function of the bladder and the bowel; the maintenance of normal muscle tone; the psychologic effect on the patient's morale and mental status; the acceleration of convalescence and the earlier return of working ability; the economic savings to the patient and the hospital.

For the reasons stated, and because of its apparent absolute safety, the plan of early postoperative ambulation seems to represent a sound surgical advance, and its more general employment in properly selected cases is recommended.

CYSTIC TUMOR OF THE ILIOPECTINEAL BURSA

REPORT OF TWO CASES

VIRGIL R. STEPHENS, M.D.
CHICAGO

Cystic enlargement of the iliopectineal bursa is comparatively uncommon. Gatch and Green [1] were able to collect only 32 cases up to 1925 in an exhaustive study of the literature. They added 1 of their own in which a woman aged 60, had a swelling in the groin about the size of a hen's egg. There were no symptoms.

Menninger [2] in 1932 reported an iliopectineal bursa the size of a goose egg in a man 36 years of age, with no history of trauma. The mass was excised and found to be communicating with the hip joint by a small opening.

In 1933 O'Connor [3] reported 33 cases of iliopectineal bursitis, in 7 of which operation was done. In at least 10 of the cases there was palpable but not necessarily visible enlargement. A good description of the symptoms and signs is given, and the methods of treatment are well outlined.

Finder [4] in 1938 described a case in which a large cystic cavity contained 500 cc. of serous fluid. It was treated by incision and drainage. The nature of the cyst was established by the finding of a small opening into the cavity of the hip joint. Muscle fibers were planted within the wide open cavity to prevent recurrence.

Two cases of cystic enlargement of the iliopectineal bursa which I have observed recently are presented herein.

REPORT OF CASES

CASE 1.—B. S., a farmer aged 73, presented himself at the MacNeal Memorial Hospital July 21, 1943, with a tender mass in the left groin, which interfered with his gait and prevented full extension of the thigh. He complained of weakness in the area of the quadriceps muscle (anterior part of the thigh) and considerable pain in that region, which prevented sleep. He had first noted symptoms there about three years previously.

A physical examination revealed normal conditions except for slight cardiac irregularity. My first impression was that he suffered from solid tumor of the bone, probably malignant. However, after roentgenograms of the hip joint were found to be normal, the mass was aspirated and yielded 25 cc. of straw-colored serous fluid, with slight relief of the symptoms. Aspiration was repeated twice, and similar amounts of fluid were withdrawn, but no subsidence in the tumor mass could be noted. The patient demanded relief, and operation was done. With the patient under general anesthesia an incision 4 inches (10 cm.) long was made diagonally downward from the anterior superior iliac spine along the medial border of the sartorius muscle. By blunt dissection the fibers of the iliacus muscle were separated down to the neck of the femur. The medial portion of the muscle along with the femoral nerve and the femoral vessels was retracted medially. The sac was separated from the surrounding tissues without any particular difficulty and found to be attached to a pedicle which was continuous with the anterior capsule of the hip joint. This pedicle was severed, but no open connection with the synovial cavity of the hip joint could be demonstrated.

The specimen which was removed showed the wall of the bursa to be about 2 to 3 mm. in thickness with a smooth synovial lining. Before deflation, it was about the size of a billiard ball and the wall consisted largely of tough white fibrous tissue. There were no calcium deposits. The wound was closed without drainage, and recovery was uneventful. All symptoms had subsided by the end of two months.

CASE 2.—M. D., a retired motorman aged 84, appeared in my office Dec. 10, 1943, complaining of severe and constant pain in the region of the right hip joint of three months' duration, with the pain radiating down to the knee; he walked with a pronounced limp. He first noted a lump in the right inguinal region one and one-half years before coming to my office. On examination a hard tumor mass, the size of a hen's egg, was seen just distal to Poupart's ligament, directly under the anterior femoral nerve. On palpation the mass appeared to be solid, and the femoral arterial pulsation over the top of the tumor suggested a possible aneurysm. However, the artery could be observed above the tumor and slightly to the medial side of its center. No fluctuation could be felt, and no fluid could be aspirated. In a second trial a week later, after attempting aspiration in four or five different places, I was finally able to secure 2 cc. of clear, slightly viscid fluid.

From the Department of Surgery, University of Illinois College of Medicine, and the MacNeal Memorial Hospital, Berwyn, Ill.

1. Gatch, W. D., and Green, W. T.: Cysts of the Ilio-Psoas Bursa, Ann. Surg. **82**:277, 1925.

2. Menninger, W.: Ueber Entzündung der Bursa Iliopectinea, Deutsche Ztschr. f. Chir. **237**:775, 1932.

3. O'Connor, D. S.: Early Recognition of Iliopectineal Bursitis, Surg., Gynec. & Obst. **57**:674, 1933.

4. Finder, J. G.: Iliopectineal Bursitis, Arch. Surg. **36**:519 (March) 1938.

Surgical excision of the tumor was then decided on. The method of approach was the same as that used in case 1, except that anesthesia was induced by preliminary administration of morphine and scopolamine and local infiltration of 1 per cent solution of procaine hydrochloride. Nitrous oxide had to be used for about five minutes during the enucleation. The sac of the bursa was not particularly adherent to the surrounding muscles, but it was attached to the anterior surface of the capsule of the hip joint by an extremely wide pedicle. The bursa was excised through the pedicle, with the production of an opening into the hip joint, through which the head of the femur could be readily palpated. This opening in the capsule of the joint was closed by two sutures. Five grams of sulfanilamide was implanted into the space where the bursa had been, as is the habit of many orthopedists, who note an occasional acute flare-up of infection in the operative field in cases of chronic bursitis. The wound was closed without drainage, there being no sign of acute inflammation present.

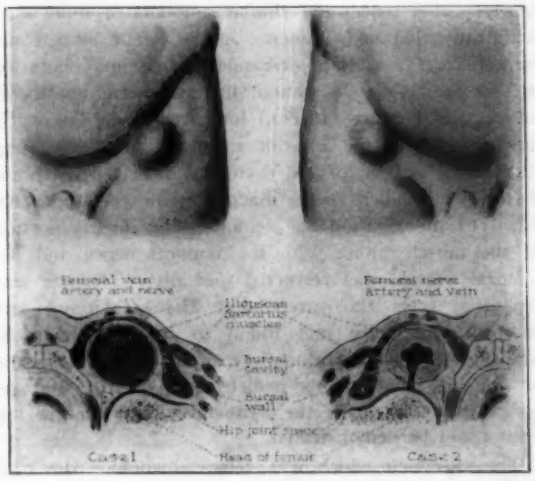


Fig. 1.—The drawings indicate the gross appearance and relationship of the cystic cavity to the hip joint, as encountered in the 2 cases herein reported. The cyst communicated with the joint in case 2 but not case 1.

The specimen which was removed was about the size of a hen's egg, the wall of which varied from 1 to 1.5 cm. in thickness. The cavity, which was of about 2 cc. capacity, was lined with apparently ordinary synovial membrane, and there were no calcified masses demonstrable in the wall of the bursa itself, which consisted mostly of a dirty, dull, wrinkled, tough fibrous mass.

Two weeks after operation tenderness and swelling appeared in the line of the incision, and a few days later a thin "mucoid" pus was obtained by thrusting a hemostat into the lower portion of the wound. A no. 18 catheter was inserted between the muscles in the track of the old incision to the cavity where fluid was collecting. Drainage lasted about two weeks, during which time the hip joint and the wound remained sensitive; the patient had no fever.

COMMENT

The 2 cases of visible enlargement of the iliopectineal bursa herein described present uncommon lesions, according to several recognized orthopedic surgeons, who when recently interviewed in regard to the matter stated that they had not seen any. The globular mass firmly fixed may be confused with an enlarged inguinal node or a femoral hernia. Aspiration of serous or seromucous fluid will differentiate it from the former, and femoral pulsation on top of the tumor will distinguish it from the latter. A psoas abscess is found in a similar location but is more fluctuant. Unilateral chronic changes in the structures of the hip joint on the involved side suggest a possible associated bursitis, particularly when other signs are present, such as tenderness over the anterior aspect of the capsule of the hip joint with pain in the region of the anterior femoral nerve.

This report is not especially concerned with the treatment of bursitis of the type represented by a small cystic tumor not associated with a joint, but in the main such treatment should be along conservative lines, as recommended by O'Connor. Cystic enlargements of various bursas may require operative treatment when they become chronically infected and do not respond to simple treatment after fair trial or when

Fig. 2.—Roentgenogram of the pelvis, showing chronic changes in the hip joint on the involved side. Chronic arthritis of the structures of the joint and atropic changes in the head of the femur are noted. A small drainage tube is shown.

they become mechanically or cosmetically a nuisance. The simplest method of intervention is aspiration followed by administration of a sclerosing agent in properly selected cases. When acute suppuration occurs, incision with or without a pack may be in order.

I have recently treated bilateral olecranon bursas and other superficial synovial sacs not connected with joints by incising, evacuating the cystic contents and inserting a small strip of

sterile gauze pack saturated with sylnasol.[5] The pack may be left one to four days, that is, until the sac is thought to be destroyed. Drainage of the excess sclerotic agent into the dressings prevents an overdosage. If desired the pack may be recharged with the sclerotic agent, with or without a needle on the syringe; the need of a recharge depends on the resistance and the thickness of the wall of the cyst. Pink drainage suggests that the wall has probably been destroyed. Healing by first intention after removal of the pack usually occurs.

5. Sylnasol is a 5 per cent solution of the sodium salts of certain of the fatty acids of the oil extracted from a seed of the psyllium group, with 2 per cent benzyl alcohol added for its anesthetic effect.

SUMMARY

Cystic tumor of the ileopectineal bursa occurred in 2 elderly men whose occupations involved strenuous use of the lower extremities. In 1 case, in which the bursa was not connected with the cavity of the hip joint, there were no corresponding changes in the structures of the hip joint. In the other case, however, in which the bursa had a wide-open communication with the cavity of the hip joint, there were distinct arthritic and atrophic changes in the structures of the joint.

CLINICAL OBSERVATIONS ON TISSUE TEMPERATURES

PATHOLOGIC AND THERAPEUTIC EFFECTS

FRANK K. SAFFORD JR., M.D., AND MAX B. NATHANSON, M.D.
NEW YORK

In the course of work on refrigeration anesthesia at New York City Hospital it seemed advisable to make studies on temperatures of tissue in order to determine: (1) the optimum temperatures necessary for satisfactory anesthesia; (2) the duration of refrigeration necessary to obtain these temperatures; (3) the minimum temperatures above which tissue must remain in order to avoid damage.

As these studies were in progress other observations became of interest, namely, the effect of the tourniquet; the optimum temperatures for prolonged refrigeration in the treatment of burns, frostbite and infections, and, finally, the temperatures that were effective and safe for reducing pain in conditions such as arthritis and neuritis.

The methods of refrigeration studied included the use of cracked ice, ice water, ice bags, electric fan plus water spray, ethyl chloride spray and mechanical refrigeration. The latter was obtained by means of a refrigerating unit [1] which cools a fluid (35 per cent alcohol) to the desired temperature—as low as 20 F.—and pumps this fluid through suitably shaped applicators of coiled metal or rubber tubing or through aluminum-finned metal tubing of a cold air chamber. A Leeds and Northrop potentiometer [2] and a thermocouple with an iron-constantan needle were used to measure temperatures. These were recorded in Fahrenheit degrees and should be accepted as approximate. The temperatures of the skin represent for the most part the mean of two or three readings.

No attempt has been made to distinguish between the commonly used terms hypothermia, crymotherapy, refrigeration, reduced temperature and cooling or between the terms describing the clinical picture of frostbite (immersion foot, trench foot, shelter foot, chilblain and erythrocyanosis). The common factor to all these terms is the implied effect of relative cold.

TEMPERATURES FOR ANESTHESIA FOR AMPUTATIONS

In order to determine optimum temperatures for satisfactory anesthesia for an amputation and the duration of refrigeration necessary to obtain these temperatures, systematic readings were made for more than 30 patients during refrigeration preliminary to the amputation. For the most part the amputations were done through the lower part of the thigh, after refrigeration produced by means of the more commonly used cracked ice pack with a tourniquet. The technic of application has been variously described.[3] Because of its greater convenience and ease of application, however, mechanical refrigeration was used whenever possible. Tables 1 and 2 show the procedure followed in measuring temperatures during each of these two technics. They also show the degree and duration of cooling necessary for what was termed "satisfactory" anesthesia. The requirements for this designation were: There should be not more than slight pain or bleeding or lowering of blood pressure during the operation, and the patient should feel able to eat a regular meal in comfort two to four hours after the operation. If slight pain was felt when the sciatic nerve was cut but there was no bleeding, the anesthesia was designated "good," as shown in table 3. In most of the cases of this study, because the degree of refrigeration was low enough and the tourniquet adequately applied, no pain was felt and no blood lost. In these cases the anes-

Dr. Lyman W. Crossman gave encouragement and advice.

This study was accomplished through the cooperation of the Physical Therapy and Surgical Divisions of New York City Hospital.

1. Made by the Therm-O-Rite Products Company, Buffalo.

2. Purchased from a fund supplied by the Council on Physical Therapy of the American Medical Association.

3. (*a*) Allen, F. M., and Crossman, L. W.: Arch. Phys. Therapy **23**:711 (Dec.) 1942. (*b*) Allen, F. M.: Anesthesiology **4**:12 (Jan.) 1943; (*c*) Anesth. & Analg. **22**:264 (Sept.-Oct.) 1943. (*d*) Crossman, L. W.; Ruggiero, W. F.; Hurley, V., and Allen, F. M.: Reduced Temperatures in Surgery: Amputations for Peripheral Vascular Disease, Arch. Surg. **44**:139 (Jan.) 1942. (*e*) Mock, H. E., and Mock, H. E., Jr.: Refrigeration Anesthesia in Amputations, J. A. M. A. **123**:13 (Sept. 4) 1943. (*f*) McElvenny, R. T.: Am. J. Surg. **58**:110 (Oct.) 1942. (*g*) Gordon, J. D.: ibid. **58**:453 (Dec.) 1942. (*h*) Kennedy, J. A.: U. S. Nav. M. Bull. **41**: 226 (Jan.) 1943. (*i*) Newman, M. K.: Arch. Phys. Therapy **24**:389 (July) 1943.

thesia was called "excellent." Such an example may be seen in table 4.

Many factors affect both the degree and the duration of refrigeration; among them are the diameter and the vascular pathologic condition of the extremity, the degree of contact between the cutaneous and refrigerating surfaces and the tightness of the tourniquet. It is preferable, therefore, to allow a margin of safety in the estimation both of the duration and of the degree of cooling. This margin is allowed for in the following temperatures and duration of refrigeration recommended for satisfactory anesthesia for amputations on the thigh:

Temperature of skin in region of operation 40 to 50 F.

Temperature of deep tissue (1½ inches [3.8 cm.] below the skin) 45 to 65 F.

Minimum duration of refrigeration three hours.

Minimum duration with a tourniquet two hours.

For amputations on thighs of large diameter and normal circulation the duration of refrigeration might preferably be longer; with reverse conditions, shorter, as shown in tables 1 and 4 respectively.

For amputations of the lower part of the leg, with a tourniquet placed below the knee, or for amputations of toes, with the tourniquet above the ankle, the duration of refrigeration would be shorter. For incisions for a paronychia, with a rubber band as a tourniquet at the base of the finger and the finger held in a glass of ice water, fifteen minutes is ample time to obtain "excellent" anesthesia. (This is demonstrated in table 5.)

By means of prolonged refrigeration anesthetic temperatures can be obtained without a tourniquet, as seen in table 3. Also anesthesia may be produced by refrigerating only the area in the neighborhood of the operating field, as demonstrated in table 4. The latter two procedures, however, were tried only once, on patients with advanced vascular pathologic conditions, and therefore are not recommended.

TEMPERATURES THAT MAY DAMAGE TISSUE

In one of the earlier papers on refrigeration Allen [4] stated that "refrigeration for more than a few hours is believed to be contra-indicated in any limb which is to be saved." He was referring to deep refrigeration by means of cracked ice and a tourniquet. In the meantime, however, the literature has frequently mentioned the possibility of prolonged deep refrigeration without perhaps enough caution regarding possible damage to tissue. McElvenny [3f] spoke of how well preserved the tissue of a leg appeared after twenty-eight days in ice. However, the leg was removed immediately thereafter, he reported. Greene [5] (two years after Allen's re-

TABLE 1.—*Refrigeration of the Whole Leg by Means of the Cracked Ice Pack*

Refrigeration for three hours (two hours with a tourniquet) preliminary to a guillotine amputation through the upper part of the thigh.

	12/21/43, 8:30 A. M. Before refrigeration; leg was exposed to room temperature for 5 minutes; cracked ice was then applied	9:30 After ½ hour's refrigeration; tourniquet was then applied; some pain was felt	11:00 After 2 hours' refrigeration	11:45 After 2¾ hours' refrigeration (2 hours with tourniquet)	12:10 P. M. Operation; some bleeding, because of high placement of tourniquet
Room temperature *	74	76	78	78	
Temperature under bed covers	89				
Rectal temperature	100	99	97.6	97	
Cutaneous temperature					
Of large toe	91.5	82	62	57.5	
Of dorsum	92.5	66.5	44	36	
Of calf	89	70	39	37.5	
Of knee	92	64.5	37	36.5	
Of upper part of thigh	87.5	68	38	38.5	
Deep tissue temperature					
In region of calf					
In subcutis ¼ in. (0.6 cm.) deep	94.5	74	44	40.5	
In muscle 1½ in. (4 cm.) deep	99	81	62	47	
In region of upper part of thigh					
In subcutis ¼ in. (0.6 cm.) deep	96.5	71	46	40.5	
In muscle 1½ in. deep	9.	86	79	59.5	

Comment.—M. H., aged 68, was treated for osteomyelitis of the left femur. The tourniquet in this case was applied forty minutes after the refrigeration was begun, in order that the leg would be somewhat anesthetized against the pain of the tourniquet. It would have been preferable to wait perhaps twice as long. Also, because of the large diameter of the patient's extremities and the necessity of placing the tourniquet high (2 inches [5 cm.] below the groin), another hour of refrigeration might have made the anesthesia "excellent." (The routine technic, more frequently followed, was to refrigerate the area of the skin where the tourniquet was to be applied by binding four uncovered ice bags to this region for thirty minutes to two hours before applying the cracked ice pack to the whole leg.) The anesthesia was designated "satisfactory."

* All temperatures are expressed in Fahrenheit degrees.

4. Allen, F. M.: Surg., Gynec. & Obst. **68**:1047 (June) 1939.

5. Greene, R.: Lancet **2**:689 (Dec. 6) 1941.

mark) recommended that a frostbitten extremity should be treated in a cold air chamber at 2 or 3 C. (36 F.) for several days or more. This recommendation was based not on actual experience with the treatment but speculatively on Lake's report that cultures of tissue survive best between 0 and 5 C (32 and 41 F.).[6] Since earlier in the same paper he had emphasized the fact that "necrosis is a vital process," it is surprising that Greene should have based a method of clinical treatment on in vitro observations.

On the basis of Greene's suggestion Davis and associates[7] treated a series of high altitude frostbites by means of cold air, at the low temperatures advised, for twenty-four to forty-eight hours. Another series of frostbites was treated by exposing the damaged parts to room temperature. The conclusion in their preliminary report was that they were not yet prepared to accept the cold air treatment. On the contrary, reasoning on the basis of Lewis'[8] statement that

TABLE 2.—*Refrigeration of the Whole Leg by Means of the Therm-O-Rite Applicator*

Refrigeration three and one half hours (two and one fourth hours with a tourniquet) preliminary to an amputation through the lower part of the thigh.

	12/10/43, 10 A. M. Before refrigeration; leg was exposed to room temperature 5 minutes; Therm-O-Rite applicator was then applied	11 A. M. After ½ hour's refrigeration; tourniquet was then applied	1 P. M. After 2½ hours' refrigeration	1:30 P. M. After 3 hours' refrigeration; operation followed at 1:45 p. m.
Room temperature	74	75	75.5	79
Rectal temperature	99	98	96.8	96.8
Temperature of Therm-O-Rite fluid	..	30		
Temperature of Therm-O-Rite applicator	..	36		
Cutaneous temperature				
Of large toe	84	62	51	49
Of dorsum	89.25	70	46.75	43
Of calf	90	59.5	41	41
Of knee	91.5	55	48	46
Of lower part of thigh	93.25	50	46	43
Deep tissue temperature of lower part of thigh				
In subcutis ¼ in. (0.6 cm.) deep	96.5	59	53	51.5
In muscle 1½ in. (4 cm.) deep	98.5	89.5	69	67

Comment.—R. H., aged 73, was treated for arteriosclerotic gangrene of the left large toe and cellulitis. The tourniquet in this case was not adequately applied (possibly because of the poor quality of rubber), with the result that some bleeding occurred. There was also slight pain when the sciatic nerve was cut. The anesthesia was therefore designated "satisfactory." For "excellent" anesthesia the temperature of 67 F. in the deep muscular tissue of the thigh was not low enough.

TABLE 3.—*Prolonged Refrigeration of the Leg by Means of the Therm-O-Rite Applicator*

Refrigeration (without a tourniquet) preliminary to an amputation through the lower part of the thigh

	12/13/43 4:00 P. M. Before refrigeration; two covered ice bags had been on foot for one week; Therm-O-Rite applicator was then applied	12/14/43 8:30 A. M. After 16 hours' refrigeration, with temperature of Therm-O-Rite fluid at 48 F.; fluid then lowered to 36 F.	10:40 After 2 hours' refrigeration at 36 F. (no tourniquet)	11:20 Operation, tourniquet was applied 5 minutes before operation; slight pain was felt when the nerve was cut; there was no bleeding	12/15/43 11:30 A. M. 24 hours later; three ice bags had been on the bandaged stump since operation; temperature of ice bag, 34 F.; cutaneous temperature of stump, 63-73 F.
Temperature of Therm-O-Rite fluid	48	48	36		
Temperature of Therm-O-Rite applicator	53	52	38		
Room temperature	71.5	..	72		
Rectal temperature	101	..	98		
Temperature of flannel-covered ice bag	39.5				
Cutaneous temperature					
Of large toe	66.5	50.5	50		
Of dorsum	83.5	46.5	48		
Of calf	94	46.5	43		
Of knee	92.25	48	42		
Of thigh	97.5	56.25	52		
Deep tissue temperature of thigh					
In subcutis ¼ in. (0.6 cm.) deep	94.5	..	48		
In muscle 1½ in. (4 cm.) deep	99.5	..	46.5		

Comment.—H. R., aged 48, suffered from gangrene of the left foot. The intention in this case was to determine how effective refrigeration anesthesia without a tourniquet might be. Moderate refrigeration (48 F.) was applied over night, followed by more intense refrigeration (36 F.) for two and three fourths hours before the operation. The temperature of 46.5 F. in the deep muscular tissue of the thigh, one half hour before operation, promised the good result that was obtained. Because of the patient's poor condition and the desirability of avoiding loss of blood, a tourniquet was applied at the last minute, while the leg was being prepared for operation. The anesthesia was designated "good."

6. Lake, N. C.: Lancet **2**:557 (Oct. 13) 1917.

7. Davis, L.; Scarff, J. E.; Rogers, N., and Dickinson, M.: Surg., Gynec. & Obst. **77**:561 (Dec.) 1943.

8. Lewis, T.: Vascular Disorders of the Limbs, London, The Macmillan Company, 1936.

"blood will not part with its oxygen if the skin is below 10 C. (50 F.)" they thought it "illogical to reduce the temperature of the already damaged tissues below 10 C."

In the course of the present study to determine what temperatures damage tissue, 3 cases of frostbite were observed. In all 3 cases frostbite followed prolonged artificial refrigeration (more than twenty-four hours). The lowest temperature of the skin recorded where blisters due to frostbite occurred was 39 F. (table 7). They never appeared during refrigeration but were first noticed twelve to forty-eight hours after the rapid warming of the part to the temperature of the bed (88 to 94 F.), following the sudden interruption of refrigeration. It is speculatively believed that all 3 might have been avoided by gradual instead of sudden warming.

CASE 7.[9]—A woman, H. P., aged 57, entered the hospital on April 18, 1943, suffering from a slight infection of the lower part of the right leg, following a blister, caused by sitting a few feet away from a stove. The patient denied that she was burned. Ten days later refrigeration was ordered because severe pyodermic infection and cellulitis of the whole lower part of the leg and the foot had developed. A large part

TABLE 4.—*Refrigeration of the Leg in the Region Between the Midthigh and the Midtibia by Means of the Cracked Ice Pack*

Refrigeration for two and one half hours (two hours with a tourniquet) preliminary to an amputation through the lower part of the thigh. The lower leg and the foot were not refrigerated.

	4/29/43, 12:45 P. M. Cracked ice applied from midthigh to midtibia	1:15 Tourniquet applied 8 in. above knee	2:45 After 2 hours' refrigeration (1½ hours with tourniquet)	3:15 Amputation through the lower part of thigh; result: "excellent" anesthesia; no pain; no bleeding
Room temperature	..	..	78	
Rectal temperature	..	..	97	
Cutaneous temperature				
Of large toe	..	..	75	
Of dorsum	..	..	72	
Of lower part of tibia	..	..	68	
Of calf	..	..	43.5	
Of thigh	..	..	40	
Deep tissue temperature in region				
Of dorsum				
In subcutis ¼ in. (0.6 cm.) deep	..	..	66	
In muscle 1 in. (2.5 cm.) deep	..	..	63	
Of calf				
In subcutis ¼ in. deep	..	..	36.5	
In muscle 1½ in (4 cm.) deep	..	..	41.5	
Of thigh				
In subcutis ¼ in. deep	..	..	36.5	
In muscle 1½ in. deep	..	..	41.5	

Comment.—W. F., aged 68, was treated for arteriosclerotic gangrene of the left foot. The intention in this case was to determine the effects of refrigeration when applied only in the neighborhood of the operating field, with the leg below this area exposed to room temperature. The patient had such thin extremities and such poor circulation that the temperature in the deeper tissues was easily and quickly lowered. The temperature of 41.5 F. in the deep muscular tissue of the thigh after two hours' refrigeration indicates that there might have been "satisfactory" anesthesia in less than two hours.

TABLE 5.—*Refrigeration of the Fingers of the Left Hand in a Glass of Ice Water*

The third finger was refrigerated without a tourniquet. The fourth finger was refrigerated with a tourniquet. The fifth finger was not refrigerated, but a tourniquet was applied. Rubber bands were used as tourniquets.

	10/22/43, 3 P. M. Before refrigeration	3:15 P. M. After 15 minutes' refrigeration	3:30 P. M. 15 minutes later (fingers out of ice water; tourniquet removed)	3:40 10 minutes later
Cutaneous temperature				
Of tip of third finger (refrigeration without tourniquet)	92.5	86.5	91.5	94
Of tip of fourth finger (refrigeration with tourniquet)	93.5	46	94.5	95
Deep tissue temperature in subcutis ¼ in. (0.6 cm.) deep	..	44.5		
Of tip of fifth finger (tourniquet without refrigeration)	93.5	71	90	94

Comment.—M. N., aged 45, reported complete anesthesia in the fourth finger. (The insertion of the thermocouple needle was not felt when the subcutaneous temperature of 44.5 F. was measured in this finger.) There was slight, if any, anesthesia in the other two fingers. Of interest was the lowering of the temperature of the skin by 22.5 F. in the fifth finger as a result of the effect of the tourniquet. This was below room temperature, because this finger was not insulated from the cooling effect of the air surrounding the ice water. Of interest, also, was the following: This patient reported marked paresthesia in his fifth finger for six weeks following the application of a tourniquet for fifteen minutes. Slight paresthesia was felt in the fourth finger for one week following the application of a tourniquet for fifteen minutes plus refrigeration. No paresthesia was felt in the third finger after the fifteen minute refrigeration without a tourniquet.

9. This patient was treated under the direction of Dr. Isidore Kross. At the critical time, it was his decision to try refrigeration therapy, in order to avoid an amputation which under the circumstances was felt might have cost the patient her life.

of the thick, swollen epidermis was separated from the underlying tissue by a profuse drainage of pus, blood and necrotic tissue. There was a strong fetid odor. The presence of the gas bacillus was suspected (later not found). She had responded to sulfathiazole, given for eight days with an increased temperature and a generalized cutaneous eruption. The temperature reached 105 F. Amputation at the thigh was considered. At this point the Therm-O-Rite applicator, with the temperature of the fluid set at 40 F., was applied.

Within fourteen hours there was a dramatic change. The temperature dropped to 99 F. The patient was comfortable. There was no pain and no odor. The drainage was less, and the tissue had become a healthy pink color.

This technic of refrigeration was continued for eleven days. The cutaneous temperatures during this period ranged between 50 and 75 F. (The latter temperature was found where two layers of petrolatum gauze acted as insulation.) The oral temperature remained near normal.

tained between 65 and 85 F., by means of the Therm-O-Rite applicator, the cracked ice pack with petrolatum gauze as insulation or, during the last two weeks, the cold air chamber again. During this period of moderate refrigeration a slow epithelization took place over the denuded surfaces of more than half of the lower part of the leg and the foot. The fourth and fifth toes sloughed off, and the stumps healed. The other toes threw off necrotic casts and healed as toes.

The cutaneous temperatures recorded during the last four weeks were never below 75 F. Twice during this period refrigeration was discontinued but, because of increased discomfort, odor and elevated oral temperature, was resumed. Finally, on the eighty-ninth day, the removal of the cold air chamber caused no untoward effects.

Comment.—In this case the points of interest to the present study were: (1) the question of burn as the cause of the initial lesion; (2) the first dramatic effect of refrigeration on the severe

TABLE 6.—*Refrigeration of the Thigh by Means of the Therm-O-Rite Applicator*

Refrigeration in order to obtain anesthesia of the muscles of the thigh while traction was applied to the contracted left leg.

	1/4/43, 11:30 A. M.	1/5/43, 11:30 A. M.	1/5/43, 3 P. M.	1/7/43, 3 P. M.
	Before refrigeration; Therm-O-Rite applicator was thereafter applied	After 24 hours' refrigeration; temperature of fluid was thereafter lowered to 32 F.	3½ hours later; refrigeration was thereafter discontinued	2 days later; leg had been exposed to temperature of bed; blisters due to frostbite appeared on thigh
Room temperature	75	73	76	75.5
Oral temperature	98.6	98	97.6	99
Temperature of Therm-O-Rite fluid	40	40 32	32	
Cutaneous temperature				
Of dorsum	90.5	82.25	76.5	94
Of calf	90.5	66	57.5	96
Of midthigh	89	62	45	94
Deep tissue temperature of midthigh				
In subcutis ¼ in. (0.6 cm.) deep	92.5	77	45	98
In muscle 1½ in. (4 cm.) deep	97	88.75	68	100.5
Angle of contracture of knee	90 degrees	160 degrees	160 degrees	

Comment.—M. M., aged 49, was treated for contracture of both legs and possible multiple sclerosis. Anesthesia was not satisfactory. Further comments on this case appear in the text.

By this time, because of the continuous drainage and because of the sweating of the cold rubber applicator, it was feared that the skin would become macerated. The cold air chamber, with the temperature of the air set at 50 F., was therefore substituted. The cooling in this chamber, however, was inadequate, either because the chamber was not kept in position or because the patient was not cooperative. On the following day the cutaneous temperatures had climbed to 82 to 92 F., the oral temperature rose and the odor returned. The Therm-O-Rite applicator was therefore reapplied, with the temperature of the fluid set at 50 F.

On the following day frostbite blisters on the knee and toes were first noticed. It was observed that these occurred wherever the weight of the applicator had added the effect of slight pressure to the effect of cold. A remark by Smith[10] that "pressure plus cold spells necrosis" and also the reports of the important role pressure plays in trench foot and immersion foot were recalled.

From this time on, for a total of eighty-nine days of refrigeration, the cutaneous temperatures were main-

infection of the limb; (3) the healthy pink flush of the skin following the first few hours of refrigeration; (4) the appearance of frostbite blisters after a brief rapid warming of the limb to the temperature of the bed, and (5) the final slow (but also dramatic in extent) epithelization and healing during over two months of moderate refrigeration.

In regard to the question of burn, reference is again made to an earlier paper by Allen.[11] Speaking of the effect of a temperature of 102 F. on the ligated limbs of rats, he remarked:

> It is astonishing to find such destructive effects of slight elevations of temperature in a water bath which feels only comfortably warm to the hand. The appearance rather strikingly resembles ordinary burns; particularly, the erythema, vesication and necrosis of limbs asphyxiated for a short time above 40° C. give an appearance which is scarcely distinguishable from that of normal limbs dipped briefly into boiling water . . .

10. Smith, L. W.: Ann. Int. Med. **17**:618 (Oct.) 1942.

11. Allen, F. M.: Am. J. Surg. **45**:459 (Sept.) 1939.

The writer witnessed one case of an arteriosclerotic diabetic whose feet were severely blistered in a Turkish bath which felt comfortable to him and his companions.

So also in this case it was believed that the patient's initial lesion was the result of exposing part of her leg, partially asphyxiated by lack of circulation, to the relatively mild heat of the stove, which caused a lesion clinically indistinguishable from a burn.

The second point of interest, namely, the dramatic effect of the first few hours of refrigeration on the severe infection of the limb, has been frequently described. Incidentally, whenever the Therm-O-Rite applicator was used purely for reducing high temperature, such as sometimes follows operation on the brain, injury of the brain or heat stroke, a dramatic lowering of temperature was easily and conveniently obtainable within a few hours. For this purpose the technic, as suggested by Fay,[12] was to place the applicator as a flat blanket under the lower part of the back, buttocks and thighs, with the temperature of the fluid at 40 F.

The third point of interest, the pink flush of the skin following exposure to cold, has also been described. In general, it is agreed that the bright color is due to the higher percentage of oxygen in the vessels, probably in part because, as Lewis observed, blood does not part with its oxygen when cooled.

Further explanation of the points of interest in this case will be offered later.

12. Fay, T.: Personal communication to the authors.

CASE 2.—The tissue temperatures recorded for the second patient in whom frostbite blisters developed during refrigeration are shown in table 6.

The intention in this case had been to obtain anesthesia of the contracted muscles of the thigh while the leg was under traction. The angle of the contracture of the knee was increased from 90 to 160 degrees, but manipulative stretching beyond this point, despite cooling, was painful. The anesthesia, therefore, was not successful, possibly because the Thermo-O-Rite applicator did not include the knee and hip.

Forty-eight hours after the refrigeration was discontinued two small frostbite blisters appeared on the lateral part of the thigh, where the lowest recorded cutaneous temperature had been 45 F. Here again the blisters probably resulted from the combination of slight pressure with moderate cold and rapid warming. They were indistinguishable from blisters caused by burns, especially those which follow the use of hot water bottles on the bloodless tissue of patients in shock.

TABLE 7.—*Prolonged Refrigeration of the Leg by Means of the Therm-O-Rite Applicator and Salted Ice*

Refrigeration preliminary to an amputation through the lower part of the thigh.

	1/18/43, 10:30 A. M.	4 P. M.	9:30	1/19/43, 10:30 A. M.	1:00 P. M.	1/20/43, 4:30 P. M.	1/31/43, 2:05 P. M.
	Before refrigeration (Therm-O-Rite then applied from knee to ankle; temperature of fluid set at 32 F.)	After 5½ hours' refrigeration; biopsy specimen 1 from calf; slight pain with incision	After 11 hours' refrigeration; biopsy specimen 2 taken from calf; no pain with incision	After 24 hours' refrigeration; patient had good night; blood oozing from incisions made for removal of biopsy specimens	After 26½ hours' refrigeration; salted ice pack put on lower area of calf for 1 hour; refrigeration then discontinued	27 hours later, without refrigeration; biopsy specimen 3 of second degree blister due to frostbite	After 4½ hours' refrigeration with Therm-O-Rite applicator (3 hours with tourniquet); amputation at 2:30; "excellent" anesthesia; biopsy specimen 4
Temperature of salted ice	..	..	..	..	28		
Temperature of Therm-O-Rite fluid	32	32	32	32	32	..	32
Temperature of Therm-O-Rite applicator	36	35	34	34	34	..	36
Room temperature	75	77	80.5	75.5	83	79.5	72.5
Oral temperature	98	98.2	98.6	98	98.6	99.4	98.6
Cutaneous temperature							
Of large toe	85	83.5	82.5	78	78	87	74
Of dorsum	92	85	85.5	77	Under salted ice 77	92	63
Of calf	91	43	39-45	39-41	Under salted ice 34	95	49.5
Of thigh	89	93	94	92.5	Under salted ice 92	91	46.5
Deep tissue temperature of calf							
In subcutis ¼ in. (0.6 cm.) deep	90.25	48	42	44	Under salted ice 36.5	97	46
In muscle 1¼ in. (3 cm.) deep	98	57.75	60	57	Under salted ice 52	99	50

Comment.—J. N., aged 65, had osteomyelitis of the left os calcis and diabetic gangrene. Further comments on this case appear in the text.

There was an interesting sequel to this treatment. A day or so later it was decided to use the Them-O-Rite applicator as a heating pad on the patient's other contracted leg in the effort, through heat, to relax the muscles of the thigh, while the leg was kept overnight in traction. The temperature of the fluid was set at 102 F. The applicator felt comfortably warm, not hot, to the patient; yet the following day two small burn blisters appeared on this leg. By this time there was no question of the exact similarity between the frostbite blisters, appearing where the cutaneous temperature was over 40 F., and the burn blisters, where the temperature could not have been over 102 F. These blisters healed in a few days with equal rapidity. Incidentally, the application of heat had also failed to correct the contracture.

CASE 3.—Table 7 describes the third case of frostbite blisters from the point of view of the tissue temperatures taken before, during and after the appearance of these lesions.

This patient had been in acute pain from the gangrenous infection of his foot. It was finally decided to amputate, but until the operation could be arranged refrigeration was applied, in order to reduce pain. Inasmuch as the patient was completely relieved of his pain within two hours, he was grateful for the prolonged refrigeration that followed and willing to allow the four biopsies.[13] The specimens for the first two biopsies were taken during refrigeration from areas of the calf where the cutaneous temperatures were 45 F. and 39 F. respectively. The specimen for the third biopsy included a frostbite blister, which in this case also had appeared after rapid warming, following prolonged refrigeration. The tissue for the fourth biopsy, taken at the time of amputation, included a blistered area that had been exposed to salted ice for one hour, during the prolonged refrigeration, and then rapidly warmed. The salted ice lowered the temperature of the skin to 34 F.

Biopsies 1 and 2 (made after refrigeration for five and one-half and eleven hours respectively).—Grossly the skin appeared bright red. Microscopically the appearance was normal.

Biopsy 3.—Gross Observations: Tissue from the left calf taken twenty-eight hours after the twenty-seven hour refrigeration was discontinued included a frostbite blister (second degree). The skin appeared as in a second degree burn but was normal outside of the blistered area.

Microscopic Observations: The surface epithelium was desquamated, with the papillary layer of the derma left exposed. The vessels were engorged and frequently contained a high polymorphonuclear content. The perivascular regions were edematous and had infiltrates of polymorphonuclear leukocytes and lymphocytes. The hair shafts and particularly the sebaceous glands were necrotic and infiltrated by degenerating polymorphonuclear cells. The surrounding area had the same type of infiltrate found in the perivascular regions. Thrombi were absent.

Biopsy 4 (made immediately after amputation).—Gross Observations: In a specimen (taken after the operation) from the lower part of the left leg, after one hours' application of salted ice the skin appeared like a third degree burn; the blister had opened and peeled off, with the underlying tissue dark red and oozing.

Microscopic Observations: The surface epithelium was denuded, with only an occasional remnant peg left. The superficial derma was degenerating and had a diffuse, slight scattering of necrotic inflammatory cells. In the deeper layers the perivascular areas had a slight polymorphonuclear and lymphocytic infiltrate. Thrombi were absent.

Comment.—What seemed significant in the latter two reports was the final statement in each: "Thrombi were absent." In other respects the reports might apply equally well as descriptions of second and third degree burns. This similarity between frostbite and burn, not infrequently observed by others, seemed worthy of more study.

Of further interest in this third case of frostbite were the low anesthetic temperatures obtained during refrigeration without a tourniquet (compare with table 3). The effectiveness of the anesthesia was well demonstrated when the biopsy specimens were taken without causing pain. We recalled Mock's [14] use of refrigeration for surface anesthesia for pinch grafts and also the anesthesia obtained by the shipwrecked sailors in the North Atlantic suffering from immersion foot. Webster [15] described their feet as "anesthetic to pain, touch and temperature."

Finally, the overnight oozing of blood during refrigeration from the incisions made for removal of the biopsy specimens seemed of interest. This prolonged bleeding as an effect of cold has been mentioned elsewhere (Allen,[3b] Lange [16]) and deserves further explanation.

Meanwhile the study of "Temperatures That May Damage Tissue" warranted the following conclusion: Cutaneous temperatures maintained below 50 F. for more than twelve hours may be damaging if contributing factors are present. These factors are: Pathologically or anatomically reduced circulation in the tissue exposed; combination of pressure with cold, and subsequent rapid warming of refrigerated tissue. It will be explained later how the last-mentioned factor is believed important and for the most part overlooked. Pressure apparently has an effect, whether it is applied to the same area as the cold or proximal to that area, as frequently happens in cases of shelter foot, trench foot and immersion foot.

Although this conclusion had been anticipated, it seemed important, because of lack of sufficient caution in the literature, to demonstrate it and emphasize it.

SUMMARY AND COMMENT

The first three aims of this study of tissue temperatures had by this time been completed: the determination of optimum temperatures for refrigeration anesthesia, the determination of the duration of refrigeration necessary to obtain these temperatures and the determination of reduced temperatures which, along with other factors, may damage tissue. The other aims, namely, the study of the effect of the tourniquet and of optimum temperatures for refrigeration used therapeutically, were but partially completed. Furthermore, a number of problems that seemed to need further elucidation had turned up, such as the prolonged bleeding as

13. The biopsy reports were obtained through the courtesy and cooperation of Dr. J. R. Lisa, pathologist at New York City Hospital.

14. Mock, H.: Bull. Am. Coll. Surgeons **28**:56, 1943.

15. Webster, D. R.; Woolhouse, F. M., and Johnson, J. L.: J. Bone & Joint Surg. **24**:785 (Oct.) 1942.

16. Lange, K.: Bull. New York M. Coll., Flower & Fifth Ave. Hosps. **5**:154 (Dec.) 1942.

an effect of cold, the bright red color of the skin following brief exposure to moderate cold, the similarity of frostbite and burn lesions, caused by 40 F. and 102 F. respectively, and the absence of thrombosis in the tissues of certain third degree frostbite lesions. The last two items involve a controversial point, that is, whether the direct effect of cold in itself may cause irreversible cellular damage or whether this damage is always secondarily the result of vasoconstriction, anoxia and subsequent warming. It was decided to offer speculative answers to these questions on the basis of this as well as of other investigations and to pursue the study further in order to try to substantiate the truth of these speculations.

In regard to the tourniquet, it is suggested that not only is the temperature of the tissue more quickly and easily lowered through the addition of the effect of the tourniquet, but because of this rapid lowering of temperature, an intermediate attempt on the part of the tissue toward a compensatory adjustment to cold is avoided and as a result perhaps less damage to surface tissue sustained, frostbite on the skin being less likely to appear. This does not imply that damage to nerves is avoided. Paresthesia, even partial paralysis, especially when cold is inadequate, may follow, as demonstrated in tables 5 and 10. Meanwhile the advantage of the tourniquet for inducing anesthesia for an amputation has become obvious.

In regard to the question of optimum temperatures for prolonged therapeutic cooling, it is suggested that an average cutaneous temperature of 70 F. is probably optimum and that in general temperatures below 80 F. and above 60 F. for prolonged treatment are more favorable than temperatures beyond these extremes. In support of this suggestion is the evidence of previous work,[17] as well as of observations on the treatment of infection and frostbite described in this study (case 1 and table 9). The optimum temperature of 70 F. is higher than that suggested by Greene,[5] lower than that recommended and used by a number of others[18] and roughly in agreement with the point of view of Rossiter,[19] who recently advised for the treatment of burn "ensuring that the skin of the burned area is kept at a temperature of 70 to 80 F."

It is further suggested that the usual custom of treating burn, frostbite and infection at room temperature, aside from being easiest, probably has no other advantage. Room temperature, obtained by means of an electric fan and water spray (recommended by Webster), as demonstrated in table 8, can be effective. As a rule, cold air, because it avoids the effects of pressure, is preferable to covered ice bags or cold appliTABLE 8.—*Refrigeration of the Lower Part of the Left Leg and Foot by Means of an Electric Fan Plus Water Spray*

	12/10/43, 9:15 A. M. Lower part of leg exposed to room temperature for 5 minutes	9:45 After 30 minutes' exposure to electric fan	10.00 After 45 minutes' exposure to electric fan; water then sprayed from atomizer	10:15 15 minutes after water spray
Cutaneous temperature				
Of toe	84	77	78	74
Of dorsum	89.5	79.5	79.5	76.5
Of calf	90	81	78	75.5
Of knee	91.5	78	78	75.5
Of thigh	93.25	82	81	76.25
Deep tissue temperature of calf				
In subcutis ¼ in. (0.6 cm.) deep	92.75	..	..	78.5
In muscle 1½ in. (4 cm.) deep	97.5	..	..	91

Comment.—R. H., aged 73, suffered from arteriosclerotic gangrene of the left toe. Because of the advanced pathologic condition of this extremity to begin with, the low temperatures quickly obtained were not thought to be a criterion of what is generally possible. Nevertheless, the effectiveness of the electric fan plus water spray, recommended by Webster and White as a method for moderate cooling, was verified.

cators of other types. The duration of treatment may vary, according to the symptomatic picture, from as short a period as minutes or hours, for different degrees of shock, to as long as months, as in the treatment described here. Finally, it is advised that by frequent measuring of tissue temperatures therapeutic cooling can be correctly guided and justified.

In regard to the bright red color of the skin following brief exposure to moderate cold, this, as has already been said, is probably due to the

17. Allen, F. M.; Crossman, L. W., and Safford, F. K., Jr.: New York State J. Med. **43**:951 (May 15) 1943.

18. (*a*) Starr, K., Jr.: Am. J. M. Sc. **187**:498 (April) 1934. (*b*) Freeman, N. E.: Influence of Temperature on Development of Gangrene in Peripheral Vascular Disease, Arch. Surg. **40**:326 (Feb.) 1940. (*c*) Ungley, C. C., and Blackwood, W.: Lancet **2**:447 (Oct. 17) 1942. (*d*) White, J. C.: New England J. Med. **228**: 213 (Feb. 18) 1943. Davis and others.[7] Webster and others.[15]

19. Rossiter, R. J.: Bull. War Med. **4**:181 (Dec.) 1943.

higher content of oxygen in the blood of the cooled area.[20] However, whether the bright color is present because oxygen does not chemically dissociate from cooled blood [21b] or also because capillary permeability is reduced [16] or because the vasoconstriction has emptied the capillaries and short-circuited the blood through arteriovenous anastomoses [21] without irrigating superficial tissue remains to be further investigated.

In regard to prolonged bleeding as an effect of cold, the theory of reduced enzymatic activity of the blood, including its coagulating process, offers probably the best explanation. This effect of cold in reducing fermentative activities, as well as tissue metabolism, apparently follows the formula [22] of van't Hoff, which implies that the speed of chemical activity is increased or decreased two or three times for every 10 C. (18 F.) rise or lowering of temperature. The importance of this law in relation to reduced tissue temperature was pointed out by Askanazy.[23]

In regard to the similarity of burn and frostbite, it should be emphasized again that because of the limited nature of past investigations answers to this question remain particularly speculative. For example, of twenty histologic studies of lesions due to reduced temperature found in the literature of the past twenty odd years, with one exception,[24] none was made on tissue subjected to biopsy or autopsy during exposure to cold. Most of the examinations were performed at least hours after the tissue had been relatively warmed. When one realizes that this warming usually involves exposing tissue which is below 40 F. to temperatures above 70 F. (a difference of at least 30 degrees) and if, keeping van't Hoff's formula in mind, one remembers how it feels to dip the hand with a normal cutaneous temperature, of 90 F., into water at a temperature of 120 F. (30 degrees difference), it is not too fantastic to assume that most of the aforementioned twenty histologic studies were made on tissues, relatively speaking, burned by the contrast of temperature. The reason that frostbite has been so frequently compared to burn becomes more clear.

In regard to the absence of thrombosis in certain frostbite lesions, if one speculates further, accepting the fact that three minutes' obstruction of an artery can produce anoxia sufficient to cause a fourfold increase in permeability of the capillaries supplied by that artery [25] and also the fact that the first reaction of the tissue to cold is neurocirculatory,[21b] namely, a local and central sympathetically controlled vasoconstriction, which may, if the cold is severe, last twenty-four hours or more [7] and may in a lower extremity, in some degree, extend to the external iliac artery,[26] one can explain most lesions due to cold on the basis of vasoconstriction, anoxia and subsequent warming alone. The absence of thrombi in many of these lesions is what distinguishes them pathologically from most burns.

In most burns capillary endothelial cells are damaged primarily less by anoxia than by the direct coagulating effect of heat, which causes formation of thrombi, typical of burned tissue. In most lesions due to cold, on the other hand, endothelial cells are damaged probably less by direct effects of temperature than by anoxia. This anoxia, depending on the contrast of the external temperature (compare the usual rapid warming following exposure to cold), may be multiplied threefold or fourfold (van't Hoff), resulting in a fourfold increase of damaging metabolites. If the cold is not too severe and the anoxia not too acute or prolonged, thrombosis may not occur. Thrombi may also not appear in the tissue of those burns which are caused by exposing asphyxiated tissue to mild heat, such as 102 F. Under such conditions the similarity of burn and frostbite becomes completely clear. According to this reasoning, the frostbite lesion usually seen and described, relatively, is a burn.

In regard to the final question of irreversibility —to continue the speculation—if one accepts the possibility that living human tissue, such as spermatozoa, can survive three hours' exposure at a temperature of —269.5 C. (—453.1 F.) (—273.1 C. [—459.6 F.] is absolute zero) or forty days at —79 C. (—110.2 F.) [27] and that the inferior vena cava of a cat may appear practically normal three weeks after it has been frozen for one minute at a temperature of —70 C.,[28] one begins to question the theory of irreversibility. On the assumption, however, that perhaps when temperatures of tissue are maintained at length somewhere between —60 C. (—76 F.)

20. Goldschmidt, S., and Light, A. B.: Am. J. Physiol. **73**:146 (June) 1925.

21. (*a*) Lewis, T.: Brit. M. J. **2**:795 (Dec. 6) 1941. (*b*) Theis, F. V.: Arch. Phys. Therapy **21**:663 (Nov.) 1940.

22. Getman, F. H.: Outline of Theoretical Chemistry, New York, John Wiley & Sons, 1928, p. 438.

23. Askanazy, M., in Aschoff, L.: Pathologische Anatomie, Jena, Gustav Fischer, 1923, vol. 1, p. 68.

24. Brooks, B., and Duncan, G. W.: Ann. Surg. **114**: 1069 (Dec.) 1941.

25. Landis, E. M.: Am. J. M. Sc. **193**:297 (March) 1937.

26. Kukin, N. N.: Arch. Sc. Biol., Moscow **62**:21, 1941.

27. Jahnel, F.: Klin. Wchnschr. **17**:1273 (Sept. 10) 1938.

28. Ebin, J.: Surg., Gynec. & Obst. **76**:43 (Jan.) 1943.

and — 5 C. (23 F.) (at which supercooled blood crystallizes [29]) an irreversible cellular necrosis does result from the direct effect of cold alone, it still remains speculative what the nature of this cellular destruction is—that is, whether it results from slower formation of larger crystals which destroy the colloidal architecture,[30] from rupture of cell membranes, from residual concentrations of sodium chloride that disturb osmotic pressure [31] or from alteration of the colloidal condition of the cell into a state more like that of a gel.[23] Further investigation will surely answer these questions.

In the realm of speculation, finally, not to be omitted, are three other factors suggested as playing a role in the pathologic effects of moderate cold: release of histamine by cold-damaged cells,[21a] local changes in acid-base balance resulting from the reduced temperature [32] and inactivation by cold of enzymes, causing an accumulation of metabolites through slow oxidation. Damage to nerves and muscles attributed to the last-mentioned factor appears to have substantiation.[33]

In view of so many uncertainties, one cannot deny the possibility of irreversible damage as a direct effect of cold, but until this has been more conclusively demonstrated one should base one's viewpoint regarding the treatment of lesions due to cold on what is more clearly discernible in the pathologic evidence: the reaction of tissue to anoxia and subsequent overwarming. One cannot fail to be impressed by Jahnel's experiments with spermatozoa or by the knowledge that fish survive being frozen solid in ice if allowed to thaw slowly or, for that matter, by the carcass meat of the mammoth that was well enough preserved to be fed to dogs after lying for thousands of years in the frozen ground of Siberia.[34] (Bacteria cultured from the trunk of this mammoth were said to resemble bacteria of today.) These are examples of the remarkable resistance of tissue, living or dead, to direct damage by cold. Whether one assumes that this direct irreversible damage is present or not, however, there still remains the secondary anoxia to be prevented or controlled by treatment.

Certainly the use of cold as treatment of lesions due to reduced temperatures would seem to be well established by its background of Eskimo folklore, the diaries of Arctic explorers, the report of Napoleon's surgeon general after experiencing a Russian winter, the comments of Lake on trench foot in the last world war, the observations of Webster, Ungley, White and others on immersion foot in this war and the recent investigations of Greene, Fay, Allen and others.

Yet, because of and despite this background, it appears necessary to reemphasize the use of cold (cutaneous temperature at 70 F.) as a primary treatment of all types of lesions due

TABLE 9.—*Mild Refrigeration (Therm-O-Rite Applicator) for Four Days of a Painful Arthritic Knee*

	4/8/43, 2 P. M. Before refrigeration (Therm-O-Rite applicator then applied)	4/9/43, 2:30 P. M. After 24 hours' refrigeration	4/10/43, 10 A. M. After 44 hours' refrigeration; temperature of fluid then lowered to 44 F.	4/12/43, 11:30 A. M. After 4 days' refrigeration; refrigeration then discontinued
Room temperature	78	78.5	75	73.5
Oral temperature	98	98.6	98.6	98
Temperature of Therm-O-Rite fluid	54	54	56 44	44
Cutaneous temperature				
Of dorsum	90.5	92.5	92	91
Of calf	85	84.5	80	83
Of knee	91.5	61	65	60
Of thigh	88.5	81.5	78	85.5
Circumference of knee	14 in. (35.6 cm.)	14 in.	14¼ in. (36.2 cm.)	17½ in. (44.5 cm.)
Motion of knee				
Angle of extension	170 degrees	170 degrees	170 degrees	170 degrees
Angle of flexion	60 degrees	60 degrees	60 degrees	60 degrees

Comment.—H. S., aged 50, suffered from swollen, painful joints, especially the left knee. Her condition was diagnosed as rheumatoid arthritis. The intention in this case was to reduce the pain of the arthritic knee by means of mild refrigeration and to observe other effects of prolonged cooling on arthritic joints. The patient reported complete loss of pain within a few hours, and thereafter a feeling of stiffness in the knee. After four days, during which the cutaneous temperature of the knee was maintained between 60 and 65 F., because of increased swelling of the knee the refrigeration was discontinued. There were no harmful after-effects. The increased swelling disappeared in a few days.

29. Lewis, T.: Brit. M. J. **2**:869 (Dec. 20) 1941.

30. Moran, T.: Proc. Roy. Soc., London s.A **112**:30, 1926. Hardy, W.: ibid. **112**:47, 1926.

31. Plank, R.; Ehrenbaum, E., and Reuter, K.: Flugshriften zur Volksernährung (Zentraleinkaufsgesellschaft), Berlin, 1917, no. 1-27.

32. Bazett, H. C., in Mock, H. E.; Pemberton, R., and Coulter, J. S.: Principles and Practice of Physical Therapy, Hagerstown, Md., W. F. Prior Company, Inc., 1935, vol. 1, p. 29.

33. Blackwood, W., and Russell, H.: Edinburgh M. J. **50**:385 (July) 1943.

34. Tolmachoff, L. P.: Tr. Am. Philos. Soc. **23**:35, 1929.

to cold, whether these are frostbite among employees of the city of New York working at temperatures as low as —20 F.,[35] of army workers in the Yukon at —75 F. or of high altitude fliers at —62 F.,[36] or immersion foot of sailors marooned in North Atlantic waters at 28 F.[12] or in Mid-Atlantic waters at 70 F.[16d] (where the night air probably lowers cutaneous temperatures of cramped wet feet below 50 F.). Other measures of treatment, such as blocking of the nerves with procaine hydrochloride and heating of the trunk to obtain reflex dilatation in the extremities, are indicated, but from the point of view of the pathologic effect they are secondary.

CONCLUSIONS

Cutaneous temperatures of 40 to 50 F. and deep muscle temperatures of 45 to 65 F. were found to give satisfactory anesthesia for amputations on the thigh. Slightly lower temperatures were necessary in order to obtain the best refrigeration anesthesia.

The minimum duration of refrigeration necessary to obtain these temperatures was found to be three hours and when the effect of the tourniquet was added at least two hours.

TABLE 10.—*Effect on the Tissue Temperature of a Tourniquet Applied Below the Knee for Three and One-Half Hours Without Refrigeration*

	12/12/42 Before Tourniquet Was Applied	3½ Hours Later
Room temperature	76	78
Oral temperature	98.6	98.2
Cutaneous temperature		
Of large toe	91.5	80
Of dorsum	93.25	83.5
Of calf	92.5	90.5
Of thigh	92.5	93.25
Deep tissue temperature of calf		
In subcutis ¼ in. (0.6 cm.) deep	94.5	92
In muscle 1½ in. (4 cm.) deep	96.5	92.25

Comment.—A tourniquet was applied to the lower part of the leg of W. J., aged 47, as a method of treating a squamous cell carcinoma. This case and the method of treatment are described in another paper, by Dr. Allen. Of interest is the drop of 10 degrees in the cutaneous temperature of the foot and the drop of 4 degrees in the temperature of the deep muscular tissue of the calf. The paralysis which followed as an effect of the tourniquet, applied for over seven hours, on this leg was anticipated. Within six months normal sensation and control of all muscles had returned.

Tissue temperatures below 50 F. for more than twelve hours may damage tissue when other factors are present. These other factors are: (1) certain types of circulatory obstruction; (2) slight pressure, and (3) subsequent warming. The last one is possibly most important.

Speculative suggestions have been offered: (1) regarding the effect of the tourniquet; (2) proposing 70 F. as the optimum average cutaneous temperature for prolonged treatment of burn, frostbite and infection; (3) regarding pathologic effects of cold that seem to justify reduced temperatures as the primary treatment of lesions due to cold.

35. Brahdy, L.: Frost-Bite Among Employees of City of New York During Winter of 1933-1934, J. A. M. A. **104**:529 (Feb. 16) 1935.

36. It has been suggested by Davis and co-workers [7] that high altitude frostbite is a unique type of cold lesion. Its appearance on the fingers one hundred to one times more often than on the cheek was posed as an inexplicable distinction. Other than the anoxemia, due to high altitudes, and the rapid changes of temperature, due to rapid flights to high altitude and back to ground again, allowing little time for compensatory adjustment on the part of the exposed tissues, it is believed that any unique quality of these lesions will be difficult to substantiate. Their predilection for fingers appears no more remarkable than the predilection of peripheral vascular disease for the extremities, where the anatomic and physiologic vascular supply is probably a more important factor than tissue mass per heat-radiating cutaneous surface.

EFFECT OF EXPERIMENTAL FRACTURE ON BONE, DENTIN AND ENAMEL

STUDY OF THE MANDIBLE AND THE INCISOR IN THE RAT

BERNARD G. SARNAT, M.D.
ST. LOUIS
AND
I. SCHOUR, D.D.S.
CHICAGO

Although there are a number of references to the clinical aspects of fractures of the jaw (Thoma, 1942 [1]; Blair and Ivy, 1936 [2]; Padgett, 1938 [3]; Major, 1943 [4]; Fry and co-workers, 1943 [5a]; Erich and Austin [5b]) relatively few experimental studies have been reported. Consequently, in view of present injuries caused by war, a roentgenographic and histologic study of the reactions of the jaw to fracture is timely. Experimental fractures of the mandible in the rat in particular permit a study of the reactions in the growing tooth as well as in the growing bone. While fractures of the jaw in dogs or guinea pigs have been studied (Schafer, 1923 [6]; Greve, 1927 [7] and Grimson, 1937 [8]), no report on the effects of fractures of the jaw in the rat and on the simultaneous reaction of all the calcified structures present at the site of fracture was found in the literature.

MATERIAL AND METHODS

This study is based on 38 rats, ranging in age from 15 to 550 days. The fracture of the mandible was unilateral in 29 animals and bilateral in 9 animals. The period of survival ranged from six and one-half hours to one hundred and fifty-eight days. Most of this material was used in a study on the effect of fractures on distant teeth (Schour in 1934 [9]).

Method of Fracturing.—The animal was anesthetized with ether and a mandible fractured by means of a small pair of cutting pliers. A clean but not a sterile technic was used. The fracture was confined to the embedded portion of the incisor just anterior to the molars or at the level of the mesial root of the first molar and was usually at right angles to the long axis of the body of the mandible and the incisor (fig. 1 *B*). Both the intraoral and the extraoral approach were used. No significant differences in results were observed. The fractured jaws were not immobilized.

The diet of the experimental animals was adequate and balanced. Part of the food was in ground form so that the temporary discomfort following the injury would not too greatly alter their capacity for intake of food. Records in respect to weight, general health, gross appearance of the mandible and incisors, state of occlusion and rate of eruption were kept throughout the postoperative life. In selected cases similar records were made previous to the operation. Occasionally roentgenograms were taken of the heads of the living animals.

Measurement of the Rate of Eruption.—The rate of eruption of the incisors was measured by making a horizontal mark with a fine file near the gingival line. With an adjustable caliper provided with fine points, the distance was measured between the point where the marking crossed the distolabial margin of the incisor and the point where the surface of the gingivae crossed the same margin. The distance between these points was measured seven days later. The difference between the two readings represented the rate of incisal eruption for that period.

Roentgenographic and Histologic Preparation.—The animals were fixed in a 5 per cent concentration of neutral solution of formaldehyde U. S. P. immediately after death. After the head was severed from the body, a midsagittal section was made to facilitate the roentgenographing of the mandible. Dental occlusal films were used. The further dissection consisted of separating the mandible and preparing it for histologic study. The pieces were washed, decalcified in 5 per cent nitric acid, followed by 5 per cent solution of sodium sulfate, embedded in celloidin and stained with

Department of Histology, University of Illinois College of Dentistry.

1. Thoma, K. H.: Traumatic Surgery of the Jaws, Including First-Aid Treatment, St. Louis, C. V. Mosby Company, 1942.

2. Blair, V. P., and Ivy, R. H.: Essentials of Oral Surgery, ed. 2, St. Louis, C. V. Mosby Company, 1936.

3. Padgett, E. C.: Surgical Diseases of the Mouth and Jaws, Philadelphia, W. B. Saunders Company, 1938.

4. Major, G.: Fractures of the Jaws and Other Facial Bones, St. Louis, C. V. Mosby Company, 1943.

5. (*a*) Fry, W. K.; Shepherd, P. R.; McLeod, A. C., and Parfitt, G. J.: The Dental Treatment of Maxillo-Facial Injuries, Oxford, Blackwell Scientific Publications, Ltd., 1943. (*b*) Erich, J. B., and Austin, L. T.: Traumatic Injuries of Facial Bones, Philadelphia, W. B. Saunders Company, 1944.

6. Schafer, H.: Ueber die Kallusbildung nach Unterkieferfrakturen, Schweiz. Monatsbl. f. Zahnh. **33:** 567-624, 1923.

7. Greve, K.: Der Heilverlauf von einfachen und komplizierten Unterkieferfrakturen mit besonderer Berücksichtigung des Mandibularkanals und der Zähne, Deutsche Zahnh. **67:**1-64, 1927.

8. Grimson, K. S.: Healing of Fractures of the Mandible and Zygoma, J. Am. Dent. A. **24:**1458-1469, 1937.

9. Schour, I.: The Effect of Tooth Injury on Other Teeth: I. The Effect of a Fracture Confined to One or Two Incisors and Their Investing Tissues upon the Other Incisors in the Rat, J. Physiol. Zool. **7:**304-329, 1934.

hematoxylin and eosin or with iron hematoxylin. The sections were mounted in serial order.

NORMAL ANATOMY AND HISTOLOGY OF THE MANDIBLE AND THE INCISOR IN THE RAT

The dentition of the rat consists of one incisor and three molars in each quadrant of the jaws. The incisor is curved, and its enamel and dentin grow and erupt continuously throughout the life of the animal. The molars, however, are of limited growth. They resemble those of man, and their enamel and dentin are completed within the first three months of life. The incisor is situated anterior to the molars in the upper jaw but extends below and beyond the molars in the mandible (fig. 10).

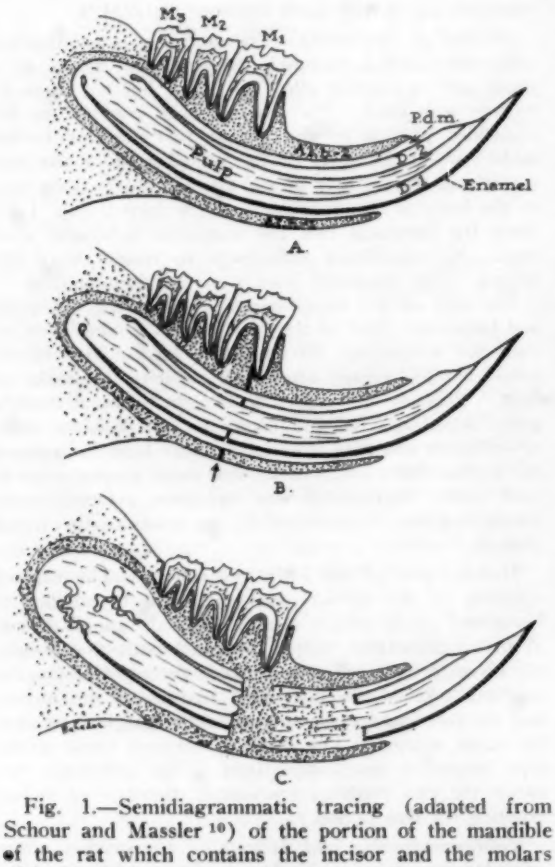


Fig. 1.—Semidiagrammatic tracing (adapted from Schour and Massler [10]) of the portion of the mandible of the rat which contains the incisor and the molars (M_1, M_2, M_3): *A*, normal structure; *B*, mandible subjected to fracture at the usual site, indicated by arrow; *C*, mandible fractured at the same site as in *B* and showing the forward movement of the anterior fragment, the ankylosis of the posterior fragment and the filling in of the region between the two segments of tooth by bone. Continued activity at the odontogenic zone has resulted in the folding of the recently formed dental tissues. *Al.b-1*, labial alveolar bone; *Al.b-2*, lingual alveolar bone; *D-1*, labial dentin covered by enamel; *D-2*, lingual dentin covered by cementum; *P.d.m.*, periodontal membrane.

A large proportion of the mandible is occupied by the incisor, and any fracture of the body of the mandible necessarily includes the incisor and its alveolar bone. A fracture of the anterior portion of the mandible in the rat, in a strict sense, is a fracture of the alveolar bone and tooth rather than of the jaw (fig. 1*A*).

Figures 1*A* and 3*a* show the lower incisor and its position in the mandible. The curvature of this tooth represents a 140 to 145 degree segment of a spiral. It has no root but consists of a long crown. The dentin constitutes the bulk of the tooth and is covered by enamel on the labial, or convex, surface and cementum on the lateral and the lingual, or concave, surface. The tooth is surrounded by fibrous connective tissue and is attached to the surrounding alveolar bone by means of the periodontal fibers. These are embedded at one end in the cementum of the tooth and at the other end in the alveolar bone. The cementum is present only on the lingual (concave) and lateral surfaces of the tooth.

In the labial portion the labial alveolar periosteum takes the place of the periodontal membrane proper. The fibers run parallel to the long axis of the tooth and fill the region between the enamel epithelium lining the enamel and the labial alveolar plate of bone. This bone is less active and occasionally shows resorption on its inner surface next to the labial alveolar periosteum. The labial bone on the external surface shows an active periosteum with apposition of bone. The bone of the mandible is of endomembranous origin. The reader is referred to an article by Schour and Massler (1942)[10] for a more detailed description of dentition in the rat in normal and in pathologic conditions.

OBSERVATIONS

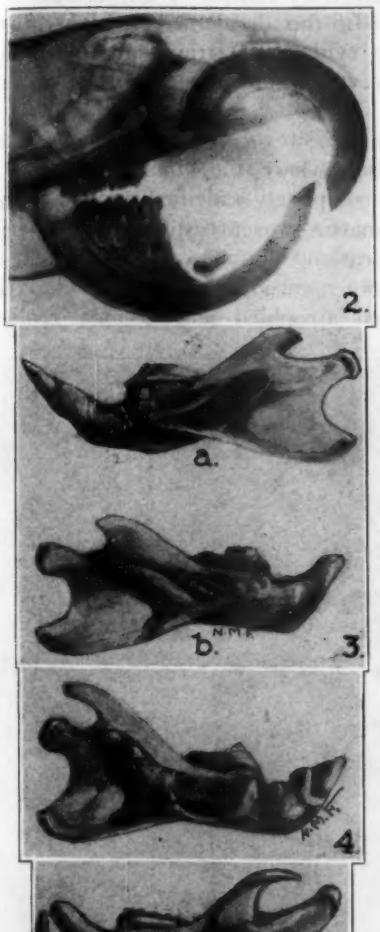
The general health of the experimental animals was, as a whole, normal and paralleled that of the controls. Most of the animals showed an uneventful recovery from the fractures. Occasionally infection was found in the region of the injury.

Because of the basic and contrasting differences in the reactions and responses to fracture of the bone and of the tooth, the observations will be described and considered under the separate headings of dental structures and bone.

REACTION OF DENTAL STRUCTURES TO FRACTURE

Gross Appearance of the Exposed Portion of the Teeth.—The appearance varied according to

10. Schour, I., and Massler, M.: The Teeth, in Griffith, J. Q., Jr., and Farris, E. J.: The Rat in Laboratory Investigation, Philadelphia, J. B. Lippincott Company, 1942.



Figs. 2 to 5.—Figure 2 is a roentgenogram of the left half of the head of rat 1, which was killed one hundred and twenty-three days after the fracture of the left mandible. Histologic sections show a persistence of a fibrocartilaginous callus in the radiolucent area, near the radiopaque area at the site of fracture. The anterior fragment of the lower incisor was lost, and the posterior fragment erupted into the oral cavity, so that it established a normal incisal relationship. Note the prominent distortion in the enamel and the partial obliteration of the pulp in the upper incisor, which also showed retarded eruption but was not fractured. × 1.8.

Figure 3 is a drawing of the left (*a*) and right (*b*) mandible of a rat which lived one hundred and forty-four days after the fracture of the right mandible. Ankylosis occurred at the site of fracture. Note in *b* the posterior extension of the right incisor to the sigmoid notch and the absence of the anterior portion of the incisor. Compare with *a*.

Figure 4 is a drawing of the right mandible of rat 73, which lived one hundred and forty-four days after its fracture. Ankylosis at the site of fracture resulted in cessation of eruption and backward growth and accumulation of the posterior portion of the incisor.

(Legend continued in next column)

the postoperative survival (figs. 3, 4 and 5). In a few of the cases, in which the anterior fragment was exfoliated, the posterior fragment perforated the lower border of the mandible (fig. 3).

The uninjured teeth became elongated in many of the animals (fig. 2). In a few animals which were operated on at an early age and had a long postoperative life (ninety-five to one hundred and fifty-seven days), the elongated upper incisors curved inwardly, so that eventually the palate was perforated.

Among those animals which showed a normal incisal relationship (that is, the incisal edges showed bevels which indicated constant normal wear), there were some in which the fractured incisor became ankylosed at the site of injury (fig. 4) and a few in which the anterior fragment was exfoliated while the posterior fragment remained in a fixed position rather than growing forward (fig. 3*b*). In the latter group, normal functional relationship was made possible because the incisor of the uninjured mandible performed the function of both lower teeth.

Gross Observations on Dissection.—The mandible showed on gross dissection characteristic disturbances, which varied with the site of fracture, the duration of the postoperative period and the condition of the anterior fragment. With the increase in the length of the postoperative life there was generally an increase in the size of the buccal protuberance of the incisor at the posterior end of the mandible. In 2 cases this protuberance was situated at the lowest level of the sigmoid notch, instead of at its normal more anterior and inferior position (fig. 3*b*). In 6 instances the posterior fragment perforated the inferior border of the mandible (fig. 5).

Rate of Eruption.—The rate of eruption of the injured incisors was retarded in all animals whose mandibles had been fractured. The retardation sometimes appeared within a week, and in some animals eruption stopped completely in a short time.

The normal standard with which the rate of eruption of the incisors of the experimental animals was compared was based on one thousand, two hundred and ten weekly measurements obtained from the following sources: (*a*) one hundred and fourteen measurements taken during the preoperative period; (*b*) three hundred and forty-three measurements taken from littermate controls, and (*c*) seven hundred and fifty-three measurements taken from normal rats.

Figure 5 is a drawing of the dissected left half of the mandible of a rat which lived one hundred and thirty-four days after the fracture of the left mandible. The exposed portion of the incisor perforated the labial alveolar bone and erupted through the cheek. Compare with the normal mandible in figure 3*a*. × 1.5.

Roentgenographic Findings.—Roentgenograms clearly demonstrated the site and the extent of the fracture (figs. 2 and 10). A thickening of the alveolar bone was sometimes seen about the site of fracture in animals of a long postoperative survival (fig. 2). The anterior fragment of the tooth was either lost or retained.

In several animals the normal radiolucent pulpal cavity was filled in and radiopaque and the width of the periodontal membrane area was increased. Buckling of the tooth in the basal area, as a result of crowding and accumulation of the calcified tissues, was common. An additional and unexpected observation was a distortion in the basal structures of the uninjured upper incisors (fig. 2).

Fig. 6.—Photomicrograph of labial portion of lower right incisor of rat 158, which was killed one hundred and thirty-two days after mandibular fracture. Note the enamel matrix which did not reach complete calcification and which is partially resorbed (*R*). The enamel matrix also shows invasion of its interprismatic substance by osteodentin (*Osd*) from the pulp. *Al.b.*, labial alveolar bone; *L.a.p.*, labial alveolar periosteum. × 144.

HISTOLOGIC OBSERVATIONS

Enamel Epithelium and Enamel.—The enamel-forming cells were completely destroyed at the site of fracture. They did not regenerate and were not replaced by adjacent reserve cells, as in the case of injury or destruction of osteoblasts. The result was that no fractured enamel was replaced by enamel or any enamel-like substitute. In the decalcified sections there was often no evidence of fragmented enamel, since the fully calcified enamel was lost in decalcification.

When the site of fracture included the posterior zone where the enamel was still in its early, incompletely calcified matrix stage, the enamel matrix was arrested during the process of calcification (fig. 6). The adjacent ameloblasts were reduced in size, or the entire enamel epithelium atrophied and became replaced by connective tissue. The enamel matrix then became covered by cementum (fig. 7) or was resorbed and replaced by osteodentin (fig. 6).

The papillary layer of the enamel epithelium occasionally responded by proliferation, as the distance from the site of injury was increased (fig. 16).

Odontoblasts and Dentin.—Either the odontoblasts at the site of fracture were permanently injured, so that formation of dentin ceased (figs. 6, 7 and 8), or they recovered. In the latter case, they deposited a peculiar type of secondary dentin, which was imperfectly formed

and calcified (fig. 6). No new generation of odontoblasts arose at the defect caused by the fracture.

The dentin itself showed no reaction to fracture, but there was a sparse infiltration of cells from the pulp and sometimes from the periodontal tissue into the region between the fragments. Eventually a fibrous union occurred between the fragments. Examination may show: (1) complete walling off by connective tissue (foreign body reaction); (2) bridging of the fragments by fibrous tissue without formation of dentin, because of the destruction of the formative cells; (3) partial resorption and replacement by osteodentin; (4) exfoliation.

Fig. 7.—Photomicrograph of the posterior portion of a midsagittal section of the lower left incisor of a rat which was killed one hundred and twenty-three days after mandibular fracture. Note the organic enamel matrix (*Org.en.*) which remained incompletely calcified and became covered with thick cementum (*Cem.*). The latter replaced the enamel epithelium. This reaction is similar to that seen in rat 166. *Al.b.*, alveolar bone; *L.a.p.*, labial alveolar periosteum; *Pred.*, predentin. (Figure taken from Schour, 1934.[9]) × 175.

Pulp.—The pulp showed a rich response, which varied with its distance from the site of fracture and with the duration of postoperative survival.

At six and one-half hours after the fracture there were profuse hemorrhage and an acute inflammatory reaction (fig. 9). Occasionally necrosis occurred (fig. 12). In one instance bone was found within the pulp four days after mandibular fracture (fig. 13). This is an unusual finding. The late reactions of the pulp were fibrosis, formation of a cyst, with cholesterol slits (fig. 8), replacement by bone, with or without hemopoiesis (fig. 14), and amorphous osteodentin, which stains irregularly and deeply with eosin (fig. 6). In spite of these alterations the basal zone of the pulp was as a rule normal and permitted continuous growth of the dental tissues (fig. 12).

In some teeth of animals of longer survival the various pulpal reactions could be seen in the same section, starting with necrosis in the anterior region where the fracture occurred and showing in sequence a zone of acute inflammation, a fibrous walling off and more posteriorly a well vascularized normal pulp.

Periodontal Membrane.—The periodontal membrane occasionally showed an excessive width. Connective tissue from the periodontal membrane frequently grew between the fragments of dentin into the pulp, producing a fibrous ankylosis. At a later stage bony ankylosis occurred (fig. 8).

Cementum.—Cementum was frequently apposed on enamel which had lost its epithelial covering and also on splinters of dentin that were implanted in a fibrous tissue (fig. 7).

Basal Zone of Incisor.—Since the sites of fracture were for the most part in the region of the first molar, direct injury of the basal zone of the incisor did not occur. However, when bony ankylosis developed at the site of fracture and eruption ceased, buckling of the posterior fragment occurred at the formative end (figs. 1*C*, 3 and 4). This accumulation resulted because the newly forming dental structures at the odontogenic zone, which normally moved forward with eruption, had become crowded at the site of their formation. In such cases there was an actual backward growth of the basal end of the tooth (figs. 3 and 4).

REACTION OF BONE TO FRACTURE

The healing reactions of the fractured bone of the mandible in the rat are generally similar to the healing reactions of bone in other parts of the body and in various species (Urist in 1942[11]).

11. Urist, M. R., and Johnson, R. W.: The Healing of Fractures in Man Under Clinical Conditions, J. Bone & Joint Surg. **25**:375-426, 1943.

The normal healing of bone may be considered in terms of the soft tissue reaction and the hard tissue reaction—or replacement by bone proper.

Our material will be described from the histologic point of view and for convenience will be described according to the following stages (table 5):

I. Procallus (hemorrhage, blood clot and organization of clot by granulation tissue) (table 1)

II. Fibrocartilaginous callus (table 2)

III. Bony callus (reorganization and architectural reconstruction of bony callus and bone) (table 3)

similar to that characteristic of inflammation. At the site of fracture the immediate reactions were those of hemorrhage, with the formation of a blood clot and a fibrin network (fig. 11). Inflammatory cells entered the field, and organization soon followed, with the invasion of granulation tissue (fig. 17). These events occurred during the first ten days. During the following week or two the granulation tissue gradually changed from a young fibrous to a mature connective tissue.

The stage of hemorrhage and the formation of the blood clot are well illustrated by rat 2, which was killed six and one-half hours after

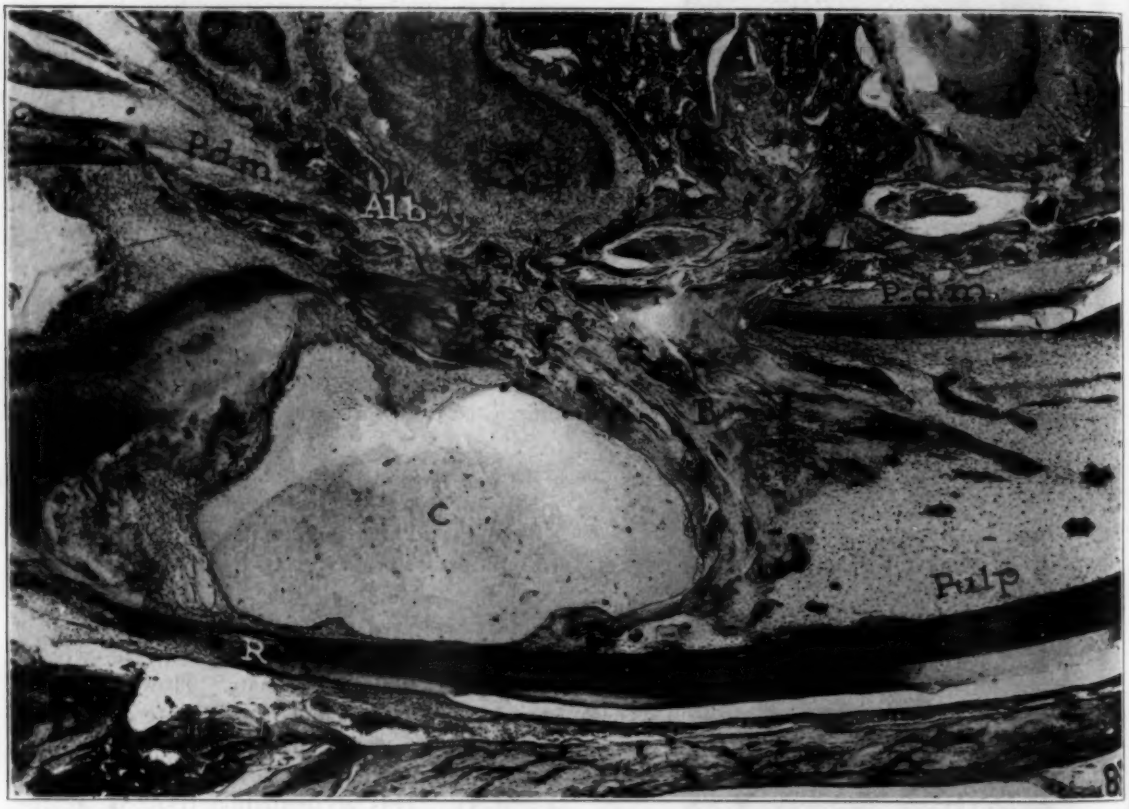


Fig. 8.—Photomicrograph of a midsagittal section of the basal portion of the lower right incisor and the mandible of rat 80, killed thirty-five days after mandibular fracture. Note pulpal cyst, *C*, with degenerative products and cholesterol slits; the union of pulpal bone, *B*, with alveolar bone, *Al.b.*, results in a bony ankylosis. The enamel matrix and the dentin are being resorbed at *R*. *P.d.m.*, periodontal membrane. × 29.

It must be pointed out that these stages are not sharply demarcated but overlap considerably. Since healing is a continuous process, any one fracture may show the predominance of a particular stage but can also indicate phases of the preceding or the succeeding stage.

Procallus.—This is the stage of healing from the period of hemorrhage to the formation of young connective tissue. A series of events occurs which is similar to that in the healing of soft tissue in the rest of the body and essentially

fracture of its mandible (table 1). Figures 9 and 10 show the site and the extent of the fracture through the bone and the tooth. A higher magnification (fig. 11) at the site of fracture of the labial bone shows the hemorrhage and the fibrin network between the fragments of bone.

A later stage, that of organization of the blood clot into granulation tissue, can be seen in histologic sections of the mandible of rat 137, which was killed three days after the mandibular fracture (figs. 15, 16 and 17). The labial bone

TABLE 1.—*Observations on Fractured Mandibles—Procallus Stage of Healing*

(Rats Arranged According to Length of Survival in Days After Fracture of Mandible)

Rat No.	Length of Survival in Days	Age at Death in Days	Clinical and Gross Observations	Roentgenographic Findings	Histologic Observations	
					Bone at Site of Fracture	Dental Structures
2 R*	¼	144	Lingual bone fractured anterior to first molar	Lingual bone fractured; labial bone intact	Lingual and labial bone fractured; hemorrhage; fibrin network	Dentin fractured with fibrin between hemorrhage in pulp
3 R	¾	144	.....	Complete fracture; displacement of lingual bone	Fibrin network; granulation tissue; round cell infiltration	Dentin not fractured
4 R	1	145	.....	.....	Early organization of clot	Enamel epithelium absent at site of fracture
5 R	2	146	.....	Comminution, with displacement of anterior portion of tooth and bone	Large amount of hemorrhage not well organized; fragments of bone	Periodontal membrane torn
137 R	3	82	.....	Labial bone fractured in region of third molar	Old hemorrhage; acute inflammatory reaction; fibrous tissue invading area	Enamel epithelium destroyed at site of fracture
65 L†	4	140	Ankylosis (?)	.....	Hemorrhage and inflammation; many fragments of bone	Pulpal reaction to trauma
65 R	4	140	.....	.....	Invasion of fibrous tissue into granulation tissue	Suppuration and necrosis of periodontal membrane; differentiation of enamel epithelium disturbed
64 L	11	147	Ankylosis (?)	Incisal portion of tooth absent	Old hemorrhage and infection; no attempt at healing	Enamel epithelium proliferating deep into connective tissue near incisal edge
144 R	16	95	Ankylosis	Irregular radiolucent areas in lingual bone	Sequestrums and infection on lingual surface	Infiltration of fibrous tissue between fragments of dentin; fibrous ankylosis
17 L	31	119	.....	Radiolucent area with radiopaque substance on lingual surface	Inflammation and hemorrhage; no healing	Deep gingival pocket with sequestrum on lingual surface

* R = right mandible.
† L = left mandible.

TABLE 2.—*Observations on Fractured Mandibles—Fibrocartilaginous Callus Stage of Healing*

(Rats Arranged According to Length of Survival in Days After Fracture of Mandible)

Rat No.	Length of Survival in Days	Age at Death in Days	Clinical and Gross Observations	Roentgenographic Findings	Histologic Observations	
					Bone at Site of Fracture	Dental Structures
64 R	11	147	.....	Complete fracture with downward displacement of anterior fragment	Old hemorrhage, dead bone and infection	
				Slight buckling of basal end of tooth	Fibrocartilage; bridging of fracture on labial surface	Slight buckling of basal end of tooth; enamel epithelium atrophied
63 R	31	141	Ankylosis; purulent drainage from mouth	.....	Fibrocartilaginous callus	Fibrous ankylosis; fragment of dentin walled off by connective tissue; infection in floor of mouth
80 R	35	94	Ankylosis	Buckling of tooth at basal end	Fibrous callus	Fibrous ankylosis; buckling of tooth at basal end; bone in pulp; cyst with cholesterol slits in pulp
58 L	47	87	.....	.....	Lingual fibrocartilaginous callus; labial bony callus	
139 L	56	108	Ankylosis	.....	Infection at site of fracture	Bone and bone marrow in pulp; incisal portion of pulp infected; hemorrhage with organization and cholesterol slits in pulp
59 L	60	100	Purulent discharge; ankylosis	Distance between fragments of bone greater than normal	Infection at site of fracture; no healing of bone	Fibrous ankylosis; old hemorrhage and infection in pulp
55 L	67	248	Ankylosis 35 days after fracture	Buckling of basal end of tooth	Bone thick; osteocartilaginous callus	Fibrous ankylosis; buckling of basal end of tooth; fibrous healing of fractured dentin
68 L	102	151	Ankylosis; purulent discharge	Bone thickened; buckling of basal end of tooth	Fibrous union; bone thick and rounded; infection in area	Fibrous ankylosis; buckling of basal end of tooth; enamel epithelium atrophied

TABLE 3.—*Observations on Fractured Mandibles—Bony Callus Stage of Healing*

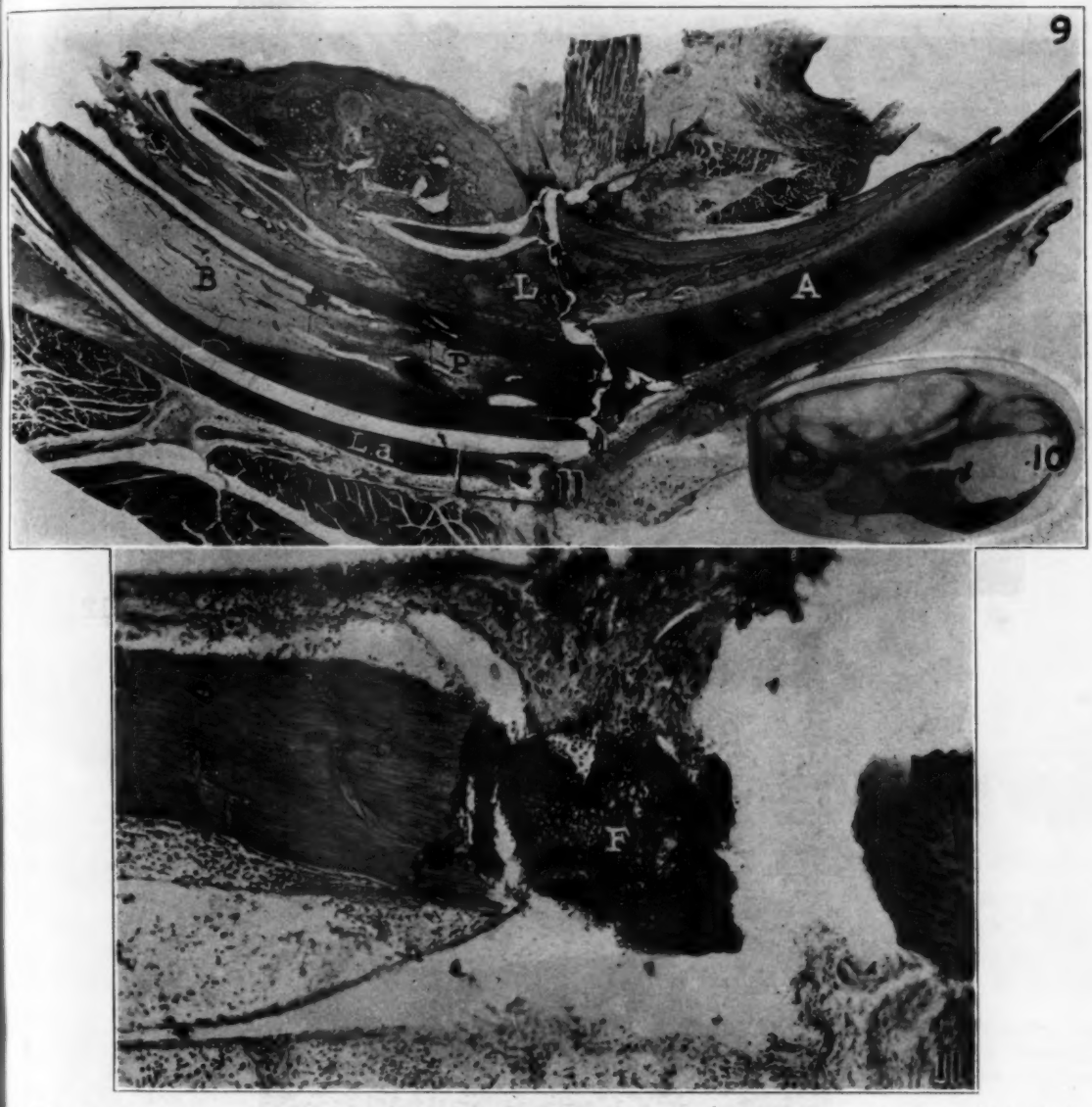
(Rats Arranged According to Length of Survival in Days After Fracture of Mandible)

Rat No.	Length of Survival in Days	Age at Death in Days	Clinical and Gross Observations	Roentgenographic Findings	Histologic Observations	
					Bone at Site of Fracture	Dental Structures
94 L	53	508	Ankylosis	No evidence of bony union	Bony union	
87 L	55	114	.....	No evidence of bony union	Bony union	Bone and bone marrow in pulp; fibrous ankylosis
51 L	59	94	.....	No evidence of bony union; pulpal cavity radiopaque	Bony union	Bony ankylosis; fibrous healing of fractured dentin; bone and bone marrow in pulp
54 R	67	187	Ankylosis	No evidence of fracture	Bony union	Bony ankylosis; bone in pulp; resorption of enamel; fragments of dentin walled off
54 L	67	187	Ankylosis	No evidence of fracture	Bony union	Bony ankylosis; bone in pulp
100 L	74	624	.....	.....	Bony union	Osteodentin; fibrous ankylosis
100 R	74	624	.....	Fragments displaced; thick callus; buckling of tooth at base	Bony union with thick callus	Buckling of tooth at base; particle of dentin walled off by bone
67 L	84	133	Ankylosis	.....	Bony union	Bony ankylosis
81 R	95	154	Ankylosis; no incisal edge	Base of tooth pushed back and buckled; no evidence of fractured bone	Bony union	Fibrous ankylosis; buckling at basal end of tooth; fibrous tissue between fragments of dentin
57 L	102	353	Ankylosis	Buckling of basal end of tooth	Bony union	Fibrous ankylosis; buckling at basal end of tooth; cementum on organic enamel matrix
57 R	102	353	Ankylosis	No roentgenographic evidence of bony union	Bony union	Fibrous ankylosis; buckling at basal end of tooth; connective tissue between fragments of dentin
82 L	109	168	Ankylosis; basal end of tooth bulged; no incisal edge	Basal end of tooth pushed backward and buckled	Bony union	Fibrous ankylosis; buckling at basal end of tooth; resorption of dentin and enamel matrix; osteodentin in pulp; only basal half of tooth present
152 R	109	124	Ankylosis	Tooth malshaped	Bony union	No evidence of active formation of tooth; fibrous ankylosis
85 L	109	168	Ankylosis; no incisal edge	Buckling of basal end of tooth; bony callus (?)	Bony union	Bony ankylosis; buckling of basal end of tooth; cementum on enamel; creeping substitution of dentin by osteodentin; bone in pulp
84 R	109	168	Ankylosis	Basal end of tooth high; buckling of tooth; obliteration of pulp	Bone grown across site of fracture	Bone and dentin in pulp; fibrous ankylosis; distortion of enamel and dentin
86 R	109	168	Ankylosis	Basal end of tooth high; marked buckling of tooth	.....	Dentin in pulp; fibrous ankylosis; cementum thickened; infection at incisal end; denticles; marked buckling of enamel and dentin
86 L	109	168	Ankylosis	Basal end of tooth high; periodontal membrane and labial alveolar periosteum wide; pulp nearly obliterated	.....	Dentin and bone in pulp; fibrous ankylosis; severe buckling of enamel and dentin; periodontal membrane wide
1 L	123	212	.....	Anterior fragment lost; posterior fragment erupted	Persistence of fibrocartilaginous callus	Cementum thickened
144 L	123	200	Ankylosis	Buckling of tooth	Bony callus; sequestrums	Ankylosis; buckling of tooth at base; osteodentin
158 R	132	192	.....	Buckling of tooth	.....	Ankylosis; buckling of tooth; serious disturbance in development of tooth; osteodentin
158 L	132	192	.....	Healing of bone; buckling of tooth	Bony callus	Ankylosis; bone in pulp; buckling of tooth
166 R	133	193	.....	Fracture healed	Fracture healed	Ankylosis; connective tissue separates fractured dentin; bone in pulp; buckling of tooth
166 L	133	193	.....	Fracture present; severe buckling of tooth	Fracture healed	Ankylosis; connective tissue separates fractured dentin; buckling of tooth
171 R	133	193	Abscess	No evidence of fracture; basal end of tooth high; pulp obliterated; buckling of tooth	No evidence of fracture	Infection in basal third of tooth; cartilage and bone in pulp
171 L	133	193	Incisor grew through wall (?)	.....	No evidence of fracture	Ankylosis; fibrous tissue with some bone between fragments of dentin
74 R	144	169	Ankylosis	Basal end of tooth	.....	Ankylosis
73 R	144	169		high; marked buckling; no evidence of fracture	No evidence of fracture	Cementicles in pulp; late complications in development of tooth
49 L	147	168	.....	No evidence of fracture; buckling of tooth	No evidence of fracture	Bony ankylosis; buckling of tooth
79 L	158	340	Ankylosis	Fracture present; buckling of tooth; pulpal cavity obliterated	Bone healed	Bony ankylosis; osteodentin; severe buckling of tooth; bone with marrow in pulp

adjacent to the site of fracture shows intense osteoblastic and osteoclastic activity (fig. 16).

Fibrocartilaginous Callus and Bony Callus.—The mature connective tissue showed evidence of formation of fibrocartilage and beginning of bony callus during the first few weeks. It was during the early part of these stages that the healing of soft tissue ended and the healing of bone began. Figures 18 and 19 show the healing of the fracture of the mandible of rat 58 (table 2). Cartilage is formed at each side of the fracture and is bridging the gap between the fragments. The central portion of the bridge contains fibrous tissue.

During the following four to eight weeks the fibrocartilaginous callus was gradually replaced

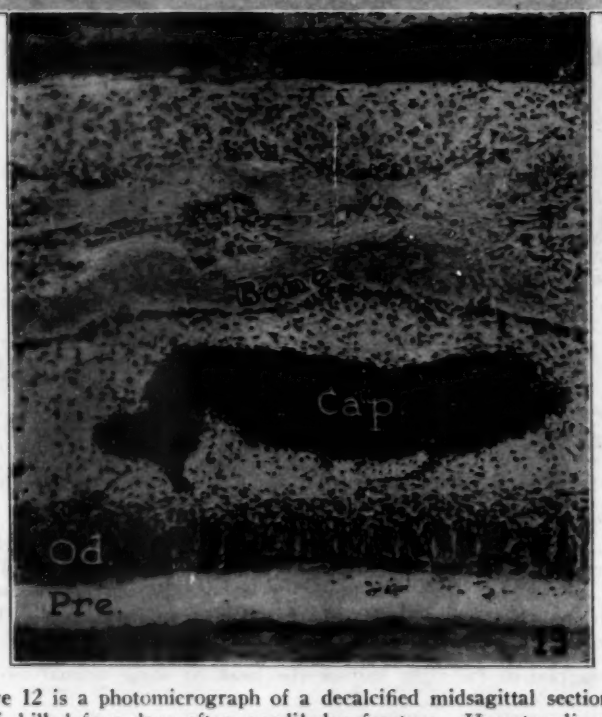


Figs. 9 to 11.—Figure 9 is a photomicrograph of a decalcified midsaggital section of the lower right incisor and the mandible of rat 2, which was killed six and one-half hours after mandibular fracture. Hematoxylin and eosin stain. Note the fracture which divided the incisor into the anterior (*A*) and posterior (*B*) fragments. The fracture is complete and extends from the lingual bone (*L*)—which is fragmented—across the tooth to the labial bone (*L.a.*). The pulp (*P*) shows hemorrhage and acute inflammation. Hemorrhage and fibrin network are seen at the site of fracture. Procallus stage (see fig. 11). ×7.

Figure 10 is a roentgenogram of the right half of the head of same animal as in figure 9. The arrow indicates the site of fracture. Natural size.

Figure 11 is a photomicrograph of the area indicated in figure 9. Note the fibrin network (*F*) at the site of fracture of the labial bone and the surrounding inflammatory reaction. Procallus stage. ×107.

by bone, and bony union of the fragments was completed (fig. 20). Figure 21 of rat 94, which was killed fifty-three days after mandibular fracture, shows two sites of fracture that have healed by bony union (table 3). In the succeeding months there was an architectural reconstruction of the bone at the site of fracture, with final healing of the bone.



Figs. 12 and 13.—Figure 12 is a photomicrograph of a decalcified midsagittal section of the lower left incisor and the mandible of rat 65, killed four days after mandibular fracture. Hematoxylin and eosin stain. Note the zones of reaction to trauma in the pulp. *1*, Fragmented dentin at the incisal edge; *2*, zone of necrosis and debris; *3*, zone of inflammatory cells; *4*, zone of hemorrhage; *5*, normal zone. Newly formed bone is seen in the pulp. See figure 13. × 7.

Figure 13 is a photomicrograph of area indicated in figure 12. The bone in the pulp is surrounded by osteoblasts and a rich amount of capillaries. Bone is seldom found in the pulp. In animals which had survived for long periods (sixty to one hundred days) after mandibular fracture there was found an ingrowth of bone. In this instance, however, the bone was present four days after fracture. Its location was a considerable distance from the site of fracture. *Od*, odontoblasts; *Pre*, predentin. × 162.

In the healing of the mandible in the rat there is usually a central bony callus and occasionally an external callus, but no internal callus. Urist (1942) [11] pointed out that in tubular bone (diaphysis) healing of the fracture is accompanied by an external and an internal callus, in addition to the central callus, but that in fractures in the region of the metaphysis there is only the simple central callus and healing occurs by the formation of intramembranous bone. The reaction in the mandible is comparable to that seen in the metaphysis.

Delay in Normal Healing of Bone.—From the time of the fracture until the final healing of bone, untoward events may occur which will delay healing. The initial step toward healing is the formation of an adequate blood clot. Consequently, any factors which tend to retard the formation of the blood clot or to disturb its organization prolong the time required for healing. Frequent causes are:

1. Displacement.

2. Mobility at the site of fracture, often leading to the persistence of the fibrocartilaginous callus.

3. Comminution of the mandible, which greatly retarded healing in several instances; frequent fibrous union, with a walling off of the fragments of dentin by fibrous tissue; sequestrums with local inflammation. There was seldom evidence of bony union.

4. Interposition of foreign tissue, particularly muscle.

5. Infection. In animal 68, in which infection was found clinically (table 2), the histologic picture revealed resorption of bone at the site of fracture, with a heavy infiltration of polymorphonuclear leukocytes.

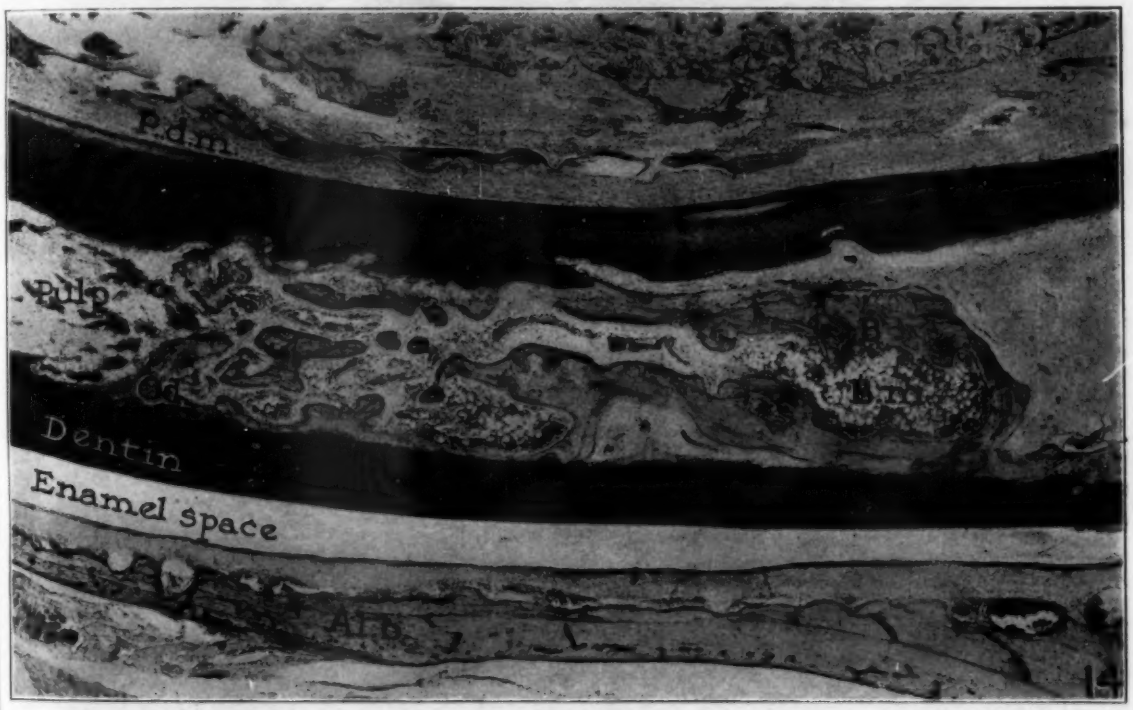


Fig. 14.—Photomicrograph of a decalcified midsagittal section of the basal third of the lower left incisor and the mandible of rat 79, killed one hundred and fifty-eight days after mandibular fracture. Note the bone (*B*) and bone marrow (*Bm*) in the pulpal cavity. In some areas the dentin is being resorbed and replaced by bone (*Od*). *Al.b.*, labial alveolar bone; *P.d.m.*, periodontal membrane. × 29.

COMMENTS

Comparison of Mandible of Rat with That of Other Species.—The mandible of the rat and the human mandible should not be strictly compared from an anatomic and a physiologic viewpoint. The relative position and the types of teeth, the distribution of bone and the origin and the insertion of muscles differ in the two species. For clinical comparison, the monkey would be a better experimental animal. Fractures of the rat mandible and of the human mandible are probably comparable only on a histologic basis. However, experimental fractures of the mandible in the rat offer a unique opportunity of studying and comparing simultaneously the effects of fracture on the growing bone and the growing tooth, and thus on all the calcified structures in the body.

Fig. 15.—Photomicrograph of a decalcified midsagittal section of the lower right incisor and the mandible of rat 137, which was killed three days after mandibular fracture. Hematoxylin and eosin stain. Note at site of fracture comminution of tooth (*C*), fractured labial alveolar bone (*La.*) and the roots of molars (*R*). × 6.5.

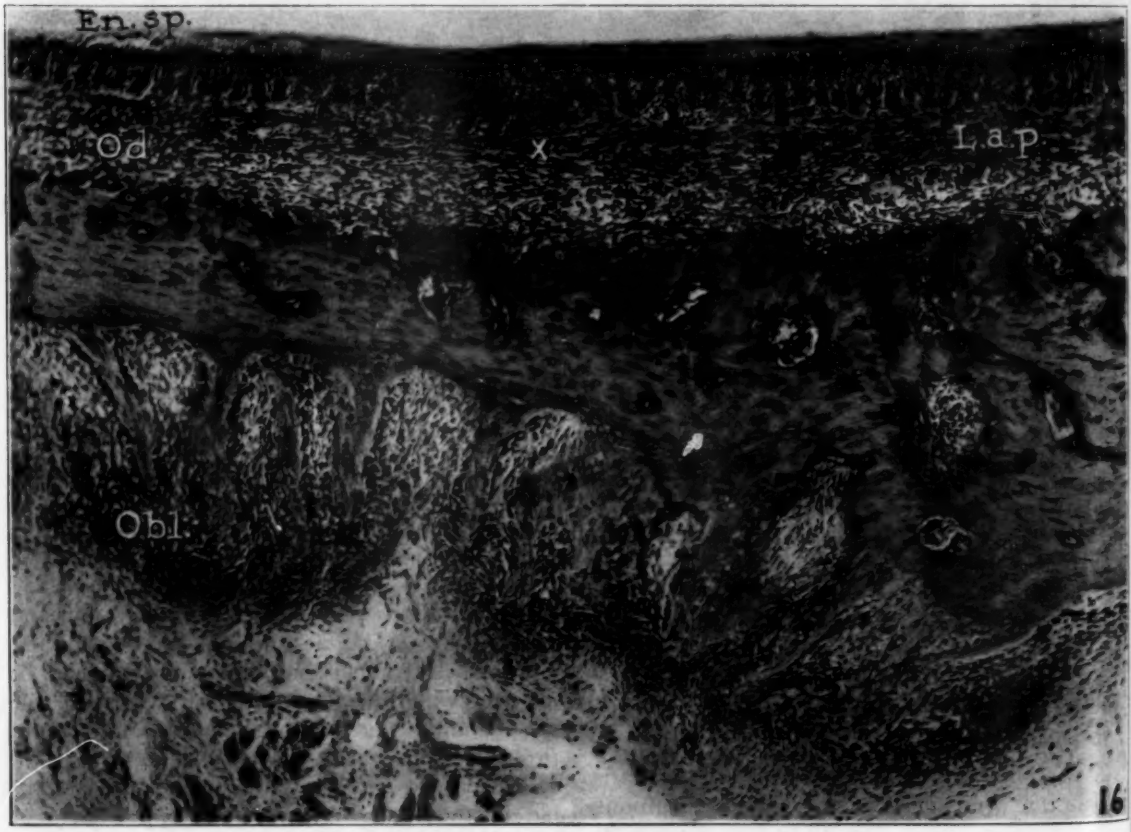


Fig. 16.—Photomicrograph of area indicated in figure 15. Note the intense osteoblastic (*Obl.*) activity on the labial surface and the intense osteoclastic (*Od.*) activity on the lingual surface of the bone adjacent to the site of fracture. The papillae of the enamel organ have proliferated at *X*. *L.a.p.*, inflamed labial alveolar periosteum adjacent to the enamel epithelium. *En.sp.*, enamel space. × 98.8.

Limited Value of Roentgenograms.—In our experiments formation of bone was demonstrated histologically during the second month, while roentgenograms did not show healing of bone until about the fourth month. In many animals for which roentgenograms showed no evidence of healing of bone, examination of the histologic sections showed that healing was well advanced. This can be explained on the basis that calcification at the site of fracture is insufficient in amount to be radiopaque. It is well known that bony union can be demonstrated earlier clinically than in roentgenograms. Roentgenograms are valuable in showing the site and the extent of fracture but are of no value in showing early healing of bone.

Periodontal Membrane and Ankylosis.—The tooth is supported in the bony alveolus by the periodontal membrane, and this type of attachment or joint is known as gomphosis. Ankylosis of this joint may occur, as of any other joint. Ankylosis of the continuously growing and erupting incisor of the mandible in the rat is frequently seen as a late complication of fracture. The ankylosis may be either fibrous, with the connective tissue of the periodontal membrane invading the pulp, or bony, with a union of alveolar bone to pulpal bone (fig. 8).

Ankylosis of the tooth, whether bony or fibrous, influences subsequent development of the tooth. The basal or growing part of the tooth is no longer able to grow forward and consequently either buckles or grows backward (figs. 3 and 4) along the course of least resistance. The anterior fragment continues to erupt and is finally exfoliated.

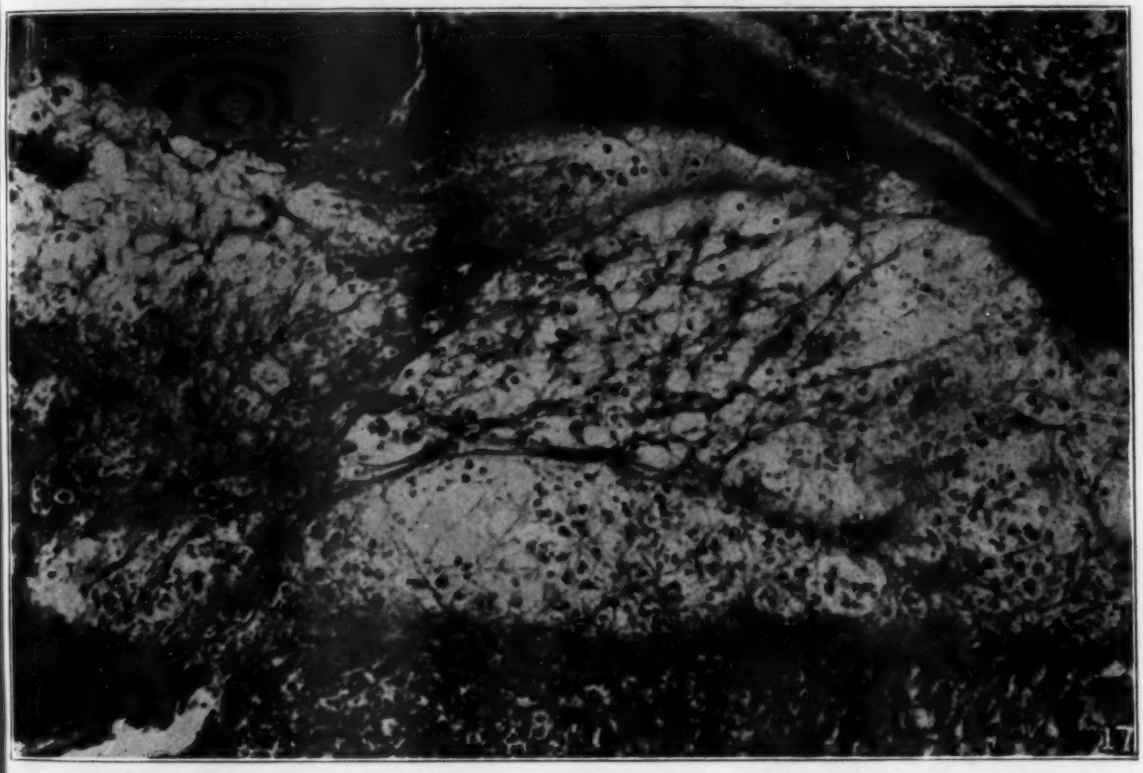


Fig. 17.—Photomicrograph of area indicated in figure 15. Note the fibrin network and the granulation tissue with leukocytic infiltration. × 305.

Comparison Between Healing of Fractures of the Jaw and Healing of Extraction Wounds.—After dental extraction bone fills the cavity left by the tooth. There is no mobility at the site as in fractures, and the area is more exposed to oral fluids and infection. Healing progresses through the same stages of blood clot, granulation tissue, mature connective tissue, healing of bone and epithelization but proceeds at a faster rate (Hubbell and Austin in 1941 [12]).

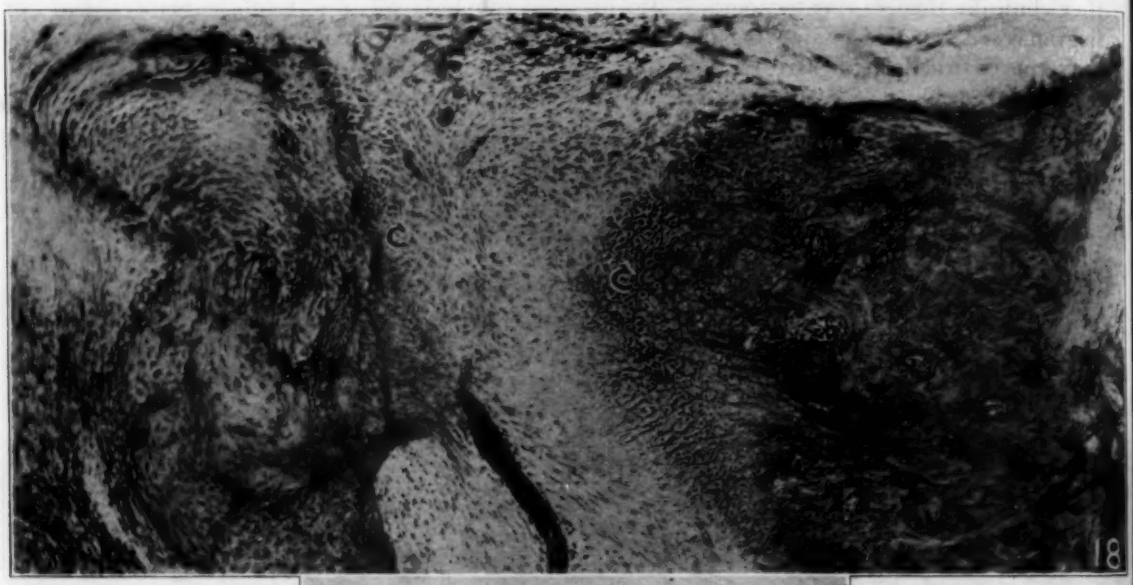
Systemic Effects of Fracture on the Growing Tooth.—This study is confined to the changes which occur in the tooth and the mandible at the site of fracture. In an earlier report (Schour, 1934 [9]), based on most of the same experimental animals, one of us (I. S.) described severe disturbances in formation of enamel and in eruption of the upper incisors (fig. 2) which were

12. Hubbell, A. O., and Austin, L. T.: Extraction Wounds and Therapeutic Agents: An Experimental Study, J. Am. Dent. A. **28**:251-258, 1941.

not injured at the time of the fracture of the lower jaw. The only explanation offered was that this distant reaction was systemic. It would be interesting to establish whether a fracture of one bone would cause lines of increased density to appear in the roentgenograms of the other growing bones.

Differences in Reaction of Various Calcified Tissues to Fracture.—In contrast to the rich reactivity and response of bone to the injury, dental tissues show little or no reaction in the enamel or the dentin but some active response in the pulp, the periodontal membrane and the cementum.

The fractured tooth changes from an actively functioning organ to one of deformity and dysfunction, while the repair of bone is frequently effective in restoration of normal function. Table 4 summarizes the striking differences in the response of bone, enamel, dentin and cementum to fractures.



Figs. 18 and 19.—Figure 18 is a photomicrograph of area indicated in figure 19. The lingual bone shows a fibrocartilaginous callus at the site of fracture. Note the cartilage cells (*C*) and the intervening fibrous connective tissue. × 99.6.

Figure 19 is a photomicrograph of a decalcified midsagittal section of the lower left incisor and the mandible of rat 58, which was killed forty-seven days after mandibular fracture. Hematoxylin and eosin stain. The effects of the fracture are shown in figures 18 and 20. Note the irregular contour of the tooth. The roots of the molars are cut tangentially. × 3.

SUMMARY AND CONCLUSIONS

This study is based on 38 rats, 29 of which were subjected to unilateral and 9 to bilateral fractures of the mandible. The animals were killed from six and one-half hours to one hundred and fifty-eight days after operation. The effects were studied in both the living and the killed animals on gross, roentgenographic and histologic bases. The mandible in the rat contains throughout its length a continuously growing and erupting incisor. Consequently, an opportunity is afforded to study the effects of fractures simultaneously on all of the different calcified structures of the body, namely, the growing bone and the growing tooth.

The roentgenograms, with few exceptions, showed little correlation with the stage of histologic repair.

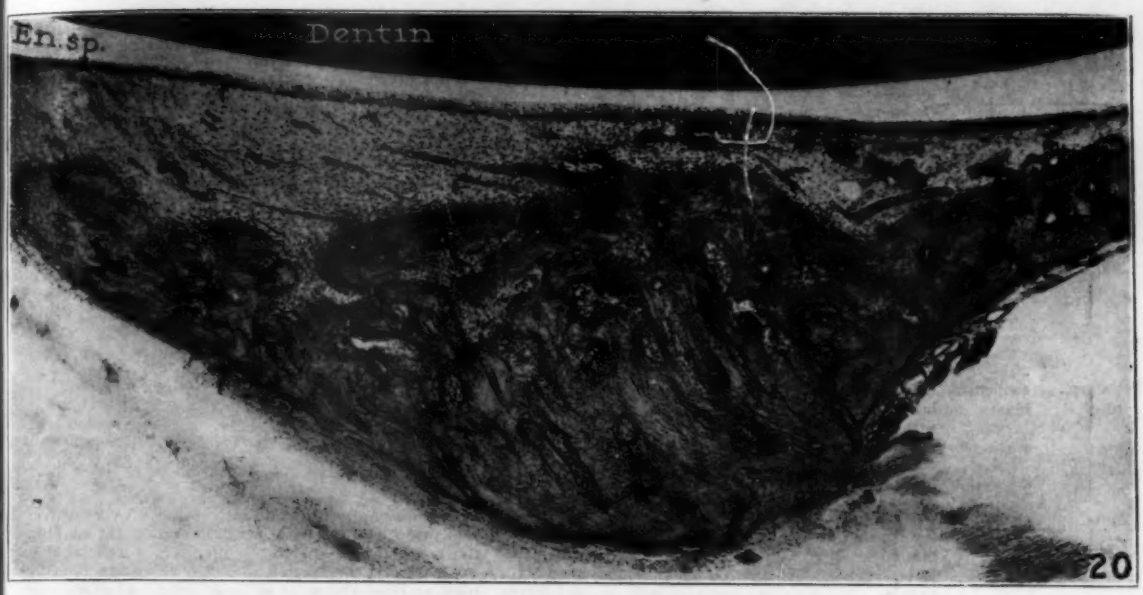


Fig. 20.—Photomicrograph of area indicated in figure 19. The labial bone shows bony union at the site of fracture, with very thick bony callus. *En.sp.*, enamel space. × 50.

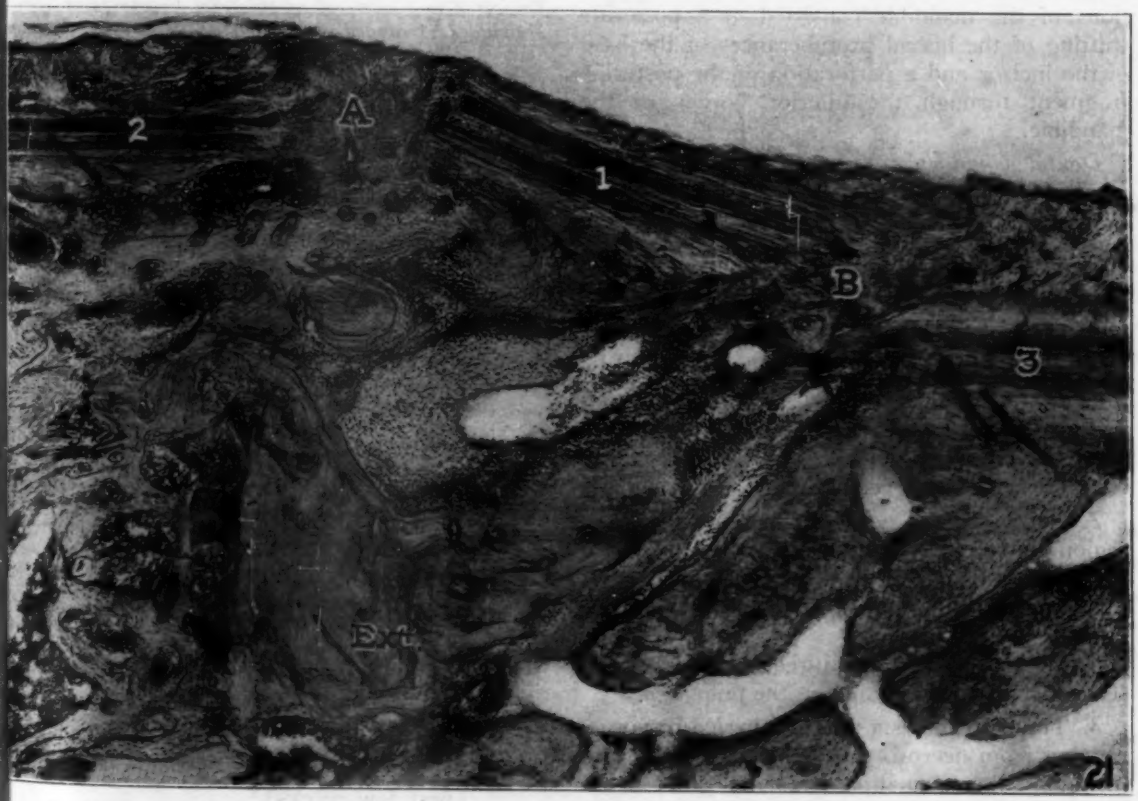


Fig. 21.—Photomicrograph of labial bone of the left mandible of rat 94, which was killed fifty-three days after mandibular fracture. Note bone fragment *1*, which was separated by fracture from bone plates *2* and *3*, and the bony union at *A* and *B*. Also note the prominent external callus, *Ext.* × 51.

TABLE 4.—*Comparison of Characteristics and Reactions of the Calcified Tissues*

	Formative Cells	Location of Formative Cells	Cellular Contents	Channels	Contents of Channels	Response to Injury in Adult Stage	Response to Injury in Growing and Calcifying Stages	Degree of Calcification: Inorganic Contents	Response to Fracture
Enamel	Ameloblasts	On surface of enamel in formative stage; absent in adult enamel	Acellular	Avascular	Physical	Entirely physical, passive, incapable of response by inflammation or regeneration; nonvital	Very sensitive to metabolic changes, leaving permanent record	97%±	Passive
Dentin	Odontoblasts	Single layer lining the pulp adjacent to most recently formed dentin	Acellular	Dentinal tubules; avascular	Protoplasmic processes of odontoblasts	Incapable of response by inflammation; can transmit stimuli through its tubules from surface of enamel to pulp	Very sensitive to metabolic changes, leaving permanent record	68%±	Passive or partial through secondary pulpal reaction
Cementum	Cementoblasts	Single layer lining the periodontal membrane adjacent to the cementum	Cement corpuscles	Canaliculi	Cementocytes	Regenerative capacity through cementoblastic properties of periodontal cells	Sensitive to metabolic changes	60%±	Partial through periodontal response
Bone	Osteoblasts	Periosteum; endosteum; lining of haversian canals	Osteocytes	Canaliculi; haversian canals; Volkmann's canals	Processes of osteocytes, vessels and nerves	Continuous apposition and resorption; rich regenerative power through osteogenic properties of periosteum and endosteum		66%±	Very active through rich cellular activity along internal and external surfaces of bone

Gross Observations.—Occasional gross distortions of the mandible consisted of a posterior shifting of the buccal protuberances of the base of the incisor and a perforation of the posterior fragment through the inferior border of the mandible.

Dental Changes.—A fractured tooth differs from a fractured bone by the absence of formation of callus and by its limited reaction. The dental structures, by contrast, are for the most part passive and nonregenerative, as follows:

1. Adult enamel reacts only mechanically and is not capable of response by inflammation or repair. The enamel matrix calcifying at the time of fracture is arrested in its calcification and shows resorption. Occasionally it loses its epithelial covering, which then is replaced by connective tissue or cementum.

2. Dentin shows no direct reaction, but the region between the fragments becomes infiltrated by cells of the pulp or the periodontal membrane. The larger fragments are joined by fibrous union.

The odontoblasts are injured, and an atypical secondary dentin is formed in the pulp.

3. The pulp shows a rich and varied response, ranging from necrosis to complete recovery and including the formation of bone and hemopoiesis.

Healing of Bone (table 5).—The stages of histologic repair of the fractured mandible in the rat may be summarized in the following chronologic order:

TABLE 5.—*Data on Thirty-Eight Rats Which Were Subjected to Unilateral or Bilateral Fractures of Their Mandibles Arranged According to Progressive Stages of Repair of Bone*

Stages	No. of Left or Right Mandibles Fractured	Period of Survival	General Histologic Characteristics	Special Comments
Procallus	10	6½ hours to 31 days	Hemorrhage; granulation tissue; young connective tissue	Roentgenographic findings show evidence of fracture (see table 1)
Fibrocartilaginous callus	8	11 to 102 days	Dense fibrous connective tissue; fibrocartilage; beginning of bony callus	Roentgenographic findings show no evidence of healing of fracture (see table 2)
Bony callus	29	53 to 158 days	Bony union; architectural reconstruction	Roentgenographic findings show variation in regard to evidence of healing of fracture (see table 3)

I. Procallus
   (*a*) Hemorrhage and initial blood clot (first few hours)
   (*b*) Organization of blood clot and invasion by granulation tissue (first few days)

II. Fibrous and/or fibrocartilaginous callus (first few weeks)

III. Bony callus (first to second month) and reorganization of bone (first year)

These events are in complete agreement with those occurring in the healing of other flat bones.

PERITONEAL TAP

LOUIS RENE KAUFMAN, M.D.; WILLIAM P. ECKES, M.D.,
AND JOSEPH MULE, M.D.
NEW YORK

Peritoneal tap affords important and useful data in the management of peritonitis. It was first performed and described by Solomon in 1906. There have been relatively few references to the procedure in the literature since that time. Contributions were made by Panichi in 1912; by Denzer in 1922 [1]; by Neuhof and Cohen in 1926 [2]; by Cole in 1937, and by Steinberg in a comprehensive paper in 1939.[3] Few of the standard textbooks even mention the procedure. Our interest in peritoneal tap was stimulated when we began an exhaustive study of perforation of peptic ulcers in an effort to reach an early definitive diagnosis by administering methylthionine chloride (methylene blue) by mouth and recovering the dye by peritoneal puncture. In a review of 89 cases of perforated peptic ulcer in the eleven years from 1930 to 1941, at the Metropolitan Hospital, McCabe and Mersheimer [4] discussed in detail the diagnosis of perforated peptic ulcer and stated that the dye had been recovered in every case in which perforation existed. This diagnostic procedure was carefully supervised by Dr. Mersheimer, and since his entrance into the naval service we have continued the procedure but have failed to recover the dye in 2 instances.

At first employed only in cases of perforated peptic ulcer, peritoneal tap is now being more generally used for a variety of conditions in which it assists in diagnosis and prognosis. Our experience has confirmed the opinion expressed by previous writers of the safety of the procedure but has emphasized the need of careful technic and interpretation of the findings.

Peritoneal tap is performed with a no. 18 or 19 gage needle, 2½ inches (6.4 cm.) long, through a small procaine hydrochloride wheal in the midline below the navel or to either side or in the epigastrium but avoiding the bladder below and, when distention is especially marked, coils of intestine which may be adherent to the anterior portion of the abdominal wall. The needle is introduced at an angle of 45 degrees, and after its point enters the peritoneal cavity it is depressed to form an angle of 15 degrees. It must be introduced with a stylet or attached to a syringe to prevent the entrance of blood during its passage through the abdominal wall. Aspiration is done by shifting the needle in various directions until fluid is withdrawn, a small amount being sufficient for examination. Gross recognition of its color and appearance, evidence of its clarity or turbidity and the presence or absence of blood, bile or extraneous matter are suggestive. Smears are made on glass slides and stained by Wright's and Gram's stains for immediate examination. Cultures are taken, but the immediate report of the smear, which is available in a few minutes, affords definite information as to the presence of gram-negative or gram-positive cocci and bacilli, the preponderant type of cells, the extent of phagocytosis and the presence of extraneous material. The technic is therefore simple, and the interpretation of the smears, while demanding rigorous accuracy, is in no way complicated. The procedure, however, is chiefly concerned with the study of the material obtained, and the laboratory data, which must be carefully and accurately recorded, are available in a few minutes. Perforation of the intestine by the needle may occur when adhesions fix the intestine to the anterior portion of the abdominal wall and the surgeon selects that particular area for peritoneal tap, but this is apparently entirely harmless. The point of the needle must be deflected, the lumen proved to be open, the position of the patient shifted and a site for the tap selected where fluid will gravitate

From the Surgical Service of the New York Medical College, the Flower and Fifth Avenue Hospital and the Metropolitan Hospital.

Presented at the Graduate Fortnight of the New York Academy of Medicine at the clinical meeting of the New York Medical College, Oct. 19, 1943.

1. Denzer, B. S.: Abdominal Puncture in the Diagnosis of Peritonitis in Childhood, J. Pediat. **8:** 741-747, 1936.

2. Neuhof, H., and Cohen, I.: Abdominal Puncture in the Diagnosis of Acute Intraperitoneal Disease, Ann. Surg. **83:**454-462, 1926.

3. Steinberg, B.: Stages in Peritonitis Based on the Defense Mechanism in Relation to Treatment, Arch. Surg. **39:**770-782 (Nov.) 1939.

4. McCabe, E. J., and Mersheimer, W. L.: Acute Gastroduodenal Perforations: Review of Metropolitan Hospital Series 1930-1941, Am. J. Surg. **62:**39-49, 1943.

or be available, which obviously in the majority of cases will be in the midline just below the umbilicus. Another site must be chosen if necessary. The amount of fluid withdrawn is immaterial, since a few drops suffices for the smear and the culture.

Steinberg [5] has established the criteria for diagnosis and for prognosis by a study of the exudate obtained, not only by peritoneal tap but through an opening in the abdomen. We desire to call attention to this study, since it is our impression that little notice is generally paid by surgeons to examination of the exudate, probably because of concentration on the clinical factors. The most significant findings are the presence and number of mesothelial cells, their viability or degeneration, the number and types of bacteria, the relative degree of phagocytosis and the presence of extraneous material (particles of food, feces or blood).

In children, peritoneal tap may be readily performed with a 2 inch (5 cm.) no. 20 gage needle and offers valuable assistance in differentiating between peritonitis due to perforating appendicitis, which is so common in children, and other forms of peritonitis, caused by such organisms as streptococci, pneumococci and gonococci. Since surgical operation is urgently indicated in perforating appendicitis and definitely contraindicated in other types of peritonitis, the procedure must be considered of value for a differential diagnosis. Denzer [1] emphasized that, in general, abdominal tap in cases of appendicitis will reveal one of the following: (1) a negative result; (2) a positive result, with no organisms on the smear and a culture which shows either no growth or a pure culture of colon bacilli or a culture of colon bacilli and a strain of coccus; (3) a positive result, with a pure culture of streptococci, which is rare. In pneumococcic peritonitis lancet-shaped diplococci with well marked capsules are recovered in a fluid that is fibrinous, slimy and greenish. In both pneumococcic and streptococcic peritonitis, there is a reduction of phagocytosis and the polymorphonuclear leukocytes are small and few in number (Steinberg [5]). However, one should never depend exclusively on the results of the tap if the weight of evidence establishes a reasonable likelihood that the child has appendicitis, in which case operation should proceed, with disregard for the negative or questionable results of peritoneal tap.

In cases of abdominal trauma, peritoneal tap may reveal blood or gross evidence of traumatic rupture of a viscus. While in the majority of cases careful clinical evaluation of the signs and symptoms is usually sufficient to arrive at a diagnosis, cases arise presenting confusion, which often leads to delay in diagnosis. In these cases operation may then reveal such significant peritoneal contents that it is certain that peritoneal tap would have furnished evidence indicating early surgical operation, with great benefit to the patient. Wright and Prigot,[6] in their review of rupture of the normal spleen, found that the spleen was involved in 47.6 per cent of cases of subcutaneous injury of the abdomen, with repeated small hemorrhage in 71 per cent of the cases. They found peritoneal tap to be of invaluable aid in the diagnosis of subcutaneous injury of the abdomen. Results of peritoneal tap proved to be positive in 13 of 15 cases of rupture of the spleen. They stated that the finding of blood by abdominal tap indicates intra-abdominal injury.

In 2 of our cases in which there was severe traumatic rupture of viscera, a peritoneal tap, although carefully performed, was completely misleading. Peritoneal tap gave positive results in 3 cases which presented diagnostic difficulties, especially in regard to determining the need for operation and the location of incision.

In cases of peritonitis, careful evaluation of the history, clinical signs, laboratory data and, especially, roentgenographic findings are in the main reliable criteria as to the cause and afford indications for or against operation. Confusion may often exist, however, because similar evidence of peritonitis will result from diversified causes, especially when distention is associated with rigidity, indefinite tenderness and a high degree of sepsis (weak, thready pulse or chemical imbalance from vomiting, dehydration). Typical examples of confusion arise in the differential diagnosis of perforated peptic ulcer, appendicitis and pancreatitis, of volvulus and mesenteric thrombosis, of rupture of solid viscera and intestine after trauma, with liability of peritonitis when delay supervenes.

Since the factor common to all types of peritonitis is the rapid formation of an exudate, an investigation of this fluid affords valuable information as to the underlying pathologic condition, especially since it is, as a rule, fairly abundant. Careful studies of the pathologic condition associated with peritonitis by Steinberg, by Hertzler, by Coller, Ransom and Rife, by

5. Steinberg, B.: Peritoneal Exudate, J. A. M. A. **116**:572-577 (Feb. 15) 1941.

6. Wright, L. T., and Prigot, A.: Traumatic Subcutaneous Rupture of the Normal Spleen, Arch. Surg. **39**:551-576 (Oct.) 1939.

Coller and Brinkman and by Meleney [7] and his associates afford definite evidence of the importance of the exudate present with peritonitis and of the value of its examination by a direct smear, indicating that this fluid obtained by peritoneal tap should provide valuable information for diagnosis and prognosis.

Hill, O'Loughlin and Stoner [8] in January 1942 reported a significant observation on dogs, confirming the value of peritoneal tap in the closed loop type of intestinal obstruction, which results in the production of the typical rusty, blood-stained fluid. Four hours after they had produced obstructed loops of bowel in the experimental animals, they were able to aspirate, by peritoneal tap, the typical reddish fluid, which showed a large number of red blood cells and bacteria, which were of diagnostic significance. In 1920, Richardson pointed out that in operations for obstruction, the findings of cherry red or pink fluid was of value in the diagnosis of strangulation of the bowel and reported its presence in 21 cases in a series of 135 cases of intestinal obstruction. Wangensteen and his co-workers described and directed attention to the phenomenon involved in the production of this typical reddish fluid. We began to study peritoneal tap more carefully about a year before the time of writing in a study of perforation of peptic ulcers by administering methylthionine chloride (methylene blue) before peritoneal tap was done to a small group of patients with suspected perforated peptic ulcers. The study was carefully controlled by Dr. Mersheimer.

In 1917, Baker [9] suggested the administration of 3 grains (0.19 Gm.) of methylthionine chloride (methylene blue) dissolved in 1 ounce (30 cc.) of water two hours before operation, so that at operation it was possible to see the blue-stained fluid in the peritoneal cavity, particularly when the admitting diagnosis was "appendicitis with peritonitis." In a later article in 1920,[10] he reported on the use of the test in 10 cases, pointing out that the method permitted "confirming the diagnosis of perforation, when the abdomen is opened, and by staining the edges of the ulcer, thus readily exposing the site of perforation."

It is interesting in connection with this technic to call attention to the suggestion of Woldman,[11] of Cleveland, commented on by Alvarez,[12] of determining the presence of a gastrointestinal lesion with a break in the mucosa by administration of phenolphthalein, dissolved first in alcohol and then in a little water; the recovery of the phenolphthalein would obviously indicate a break in the mucous membrane. Banks and Barron [13] in 1939 reported on the use of this method on 52 patients with intrinsic lesions of the gastrointestinal tract and on 151 controls with a variety of conditions or with no demonstrable organic disease. This method, of course, is not suitable for diagnosis of perforation but affords an interesting background for the use of dye tests in diagnosis.

The absence of free gas, demonstrated roentgenographically, which furnishes evidence of peritonitis, with pain and tenderness in the right lower quadrant of the abdomen from spillage of the escaped gastric or duodenal contents along the right gutter, frequently leads to a diagnosis of perforating appendicitis. In such cases, exploratory operation requires a long rectus incision prolonged beyond the limit we deem wise (short upper right rectus incision or muscle splitting incision) for perforated peptic ulcer. Our experience has encouraged us to continue this diagnostic procedure, which is simple, safe and definitely useful if carefully performed. The most common failure is failure to obtain any fluid (dry tap) when operation a few hours later demonstrates its presence.

In that considerable group of cases in which peritonitis rapidly develops shortly after the onset of abdominal pain, determination as soon as possible of the precise pathologic condition is the first consideration for proper treatment. While evidence of peritonitis is conclusive, continuing gastrointestinal distention soon increases the difficulty of diagnosis by palpation and percussion. Peritoneal tap will be of practical assistance in reaching a decision as to the need for surgical intervention and the site of the incision. From careful study of the data obtained by peritoneal tap, further diagnostic evidence

7. Meleney, F. L.; Harvey, H. D., and Jern, H. Z.: Peritonitis: I. The Correlation of the Bacteriology of the Peritoneal Exudate and the Clinical Course of the Disease in 106 Cases of Peritonitis, Arch. Surg. **22**: 1-66 (Jan.) 1931.

8. Hill, F. C.; O'Loughlin, B. J., and Stoner, M.: Peritoneal Aspiration in the Diagnosis of Strangulated Bowel, Surg., Gynec. & Obst. **74**:121-123, 1942.

9. Baker, H. L.: Methylene Blue in the Diagnosis of Acute Perforating Gastric and Duodenal Ulcers, Surg., Gynec. & Obst. **25**:695, 1917.

10. Baker, H. L.: Methylene Blue in the Diagnosis of Acute Perforating Gastric and Duodenal Ulcers, Surg., Gynec. & Obst. **30**:93, 1920.

11. Woldman, E. E.: A Simple Test for Determining the Presence of Gastrointestinal Lesions: A Preliminary Report, Am. J. Digest. Dis. **5**:221-224, 1938.

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TABLE 1.—*Summary of Twenty-Two Cases in Which Peritoneal Tap Was Done*

Name, Sex, Age	Preoperative Diagnosis	Location of Peritoneal Tap	Result	Roentgenogram	Postoperative Diagnosis
J. R., M, 15	Ruptured spleen	Both lower abdominal quadrants	Bloody fluid; no bacteria; many R. B. C. and W. B. C.	None	Traumatic rupture of spleen
L. R., M, 36	Ruptured viscus; ruptured spleen	Right lower abdominal quadrant	Serosanguineous fluid; no organisms in smear; many R. B. C.; moderate number of W. B. C.; culture negative after 48 hr.	No gas or subdiaphragmatic air present	Laceration and severance of terminal portion of ileum; fecal peritonitis
F. T., M, 65	Ruptured viscus with peritonitis	Lower part of abdomen	Doubtful	Subdiaphragmatic air present	Perforation of duodenal ulcer with peritonitis
J. B., M, 52	Ruptured viscus with peritonitis	Lower part of abdomen	Negative	Subdiaphragmatic air present	Rupture in terminal portion of ileum; tear in its mesentery
J. R., M, 51	Ruptured ulcer; peritonitis	2 in. below and to left of midline	Small amount of serosanguineous fluid; no methylene blue	None	Rupture in prepyloric region of lesser curvature; ulcer of stomach
J. O., M, 34	Ruptured peptic ulcer	Midline at epigastrium	Dry tap	No subdiaphragmatic air present	Rupture at pylorus on anterior surface of stomach near lesser curvature; methylene blue seen escaping from rupture during operation
A. K., M, 54	Ruptured duodenal ulcer; methylene blue test	Right upper and right lower abdominal quadrants	From right upper abdominal quadrant, negative; from right lower quadrant, clear amber fluid; no methylene blue	None	Ruptured prepyloric ulcer
H. K., M, 51	Ruptured duodenal ulcer; methylene blue test	Lower part of abdomen	Milky white fluid; polymorphonuclear cells with many bacteria	None	Ruptured prepyloric ulcer
J. S., M, 28	Ruptured duodenal ulcer; methylene blue test	Right lower abdominal quadrant	Methylene blue	None	Ruptured gastric ulcer
J. O., M, 42	Ruptured duodenal ulcer; methylene blue test	Right lower abdominal quadrant	Methylene blue	None	Ruptured duodenal ulcer
A. B., M, 37	Ruptured duodenal ulcer; methylene blue test	Right lower abdominal quadrant	Methylene blue	None	Ruptured duodenal ulcer
C. O., M, 43	Ruptured duodenal ulcer; methylene blue test	Right lower abdominal quadrant	Methylene blue	None	Ruptured duodenal ulcer
M. M., M, 55	Ruptured malignant growth of stomach	Lower part of abdomen	Small amount of serosanguineous fluid; no methylene blue	Subdiaphragmatic air present	Ruptured carcinoma of stomach
A. A., M, 50	Ruptured bowel	Lower part of abdomen	Feces	Normal	Traumatic rupture of spleen with hemorrhage
F. K., M, 28	Possible intraperitoneal hemorrhage	Left of umbilicus	Dry tap	None	No operation; patient well when released
T. J., M, 54	Diffuse peritonitis	2 in. below and to left of umbilicus	Few drops of brown cloudy fluid; predominant polymorphonuclear cells on smear; neutrophils; many foci of degenerative forms; suspicious colonies of bacteria	None	Laparotomy; abdomen contained 500 cc. of brown fluid; diffuse peritonitis; diverticulitis of cecum
A. J., M, 65	Peritonitis	2 in. below and to left of umbilicus	0.5 cc. of cloudy white fluid; smear, 100 per cent neutrophils; many degenerative forms	No subdiaphragmatic air present	Carcinoma of head of pancreas with pancreatitis and peritonitis
C. F., F, 65	Intestinal obstruction; peritonitis	2 in. below and to left of umbilicus	Foul smell; cloudy fluid	None	Perforated diverticulum of sigmoid; local abscess and obstruction
J. M., F, 54	Carcinoma of rectosigmoid with intestinal obstruction	Right lower abdominal quadrant	Feces with Bacillus coli and Bacillus aerogenes	Intestinal obstruction	Carcinoma of sigmoid with gangrene of large bowel and intestinal obstruction
E. C., F, 51	Rupture of stomach; peritonitis	Lower part of abdomen	Doubtful	Subdiaphragmatic air present	Ruptured prepyloric ulcer
E. C., F, 68	Abscess in pelvis	Right of umbilicus	5 cc. of faintly turbid fluid; shreds of mucus; smear containing many diplococci, short-chained streptococci; predominant cells, lymphocytes	None	Abscess in pelvis of undetermined origin
I. H., F, 38	Postoperative adhesions; pancreatitis	Lower part of abdomen	Negative	None	Cholecystitis with adhesions

will be accumulated, which should be of decided value in treatment.

Peritoneal tap may be accepted as a safe procedure, since penetration of intestine or any blood vessel is almost impossible, but if it occurs no harm results. We have twice penetrated the intestine, once the cecum and once the terminal portion of the ileum, and both times we obtained direct fecal material; then we demonstrated at operation a few hours later the site of penetration, which was apparently well sealed by the exudate. Recent experience with the procedure has demonstrated its value in the treatment of postoperative complication of peritonitis. In 1 case, after cholecystectomy, peritoneal tap showed the presence of free bile long before we should have recognized a leaking cystic duct as the cause of unexplained distention. In another case five days after resection of the descending colon with axial anastomosis, evidence of peritonitis developed, and a tap, performed in the left lower part of the abdomen, revealed fecal-stained fluid. The incision was reopened and the area segregated, with the result a controlled fecal fistula and recovery of the patient.

In our service at both the Flower and Fith Avenue Hospital and the Metropolitan Hospital, we have performed about 40 peritoneal taps in the last two years without any complications. A careful study of the procedure was begun in the winter of 1943 in a group of 22 cases (table 1). There were 18 men and 4 women, varying in age from 28 to 65. No patients with suspected appendicitis were subjected to peritoneal tap, since it is our rule to proceed as directly as possible to immediate operation on such patients. The group of cases in which peritoneal tap was done presented diagnostic difficulties in determining the cause of the peritonitis and required exploratory laparotomy for final diagnosis. Peritoneal tap in this group of 22 cases yielded information of definite value in diagnosis and treatment in 14 cases (63.6 per cent) and was found to give negative results or to be misleading in 6 cases (27.2 per cent) and to be of doubtful value in 2 cases (9.2 per cent).

CONCLUSIONS

Peritoneal tap is a practical and safe procedure which requires meticulous care in removal of the peritoneal contents and study of the smears and which affords evidence, by a simple and rapid laboratory study, of the peritoneal reaction present.

In children, the procedure serves to differentiate streptococcic and pneumococcic peritonitis from appendicitis.

TABLE 2.—*Results of Peritoneal Tap in Twenty-Two Cases*

Diagnosis	No. of Cases	Positive Results of Tap	Doubtful Results of Tap	Negative Results of Tap	Comment
Perforated peptic ulcer	10	7	2	1	Total number of cases 22 Youngest patient 28 years Oldest patient 65 years Men 11 Woman 1
Intraperitoneal hemorrhage	2	1	1	..	Presumption of bleeding; dry tap; recovery without operation
Perforated carcinoma of stomach	1	1			
Perforated carcinoma of rectosigmoid	1	..	..	1	Puncture of distended rectosigmoid proved by operation
Pancreatitis	1	1			
Traumatic rupture of spleen	2	1	..	1	Puncture of intestine; results of tap misleading; free blood present not recovered
Traumatic rupture of ileum	2	1	..	1	In 1 case, tap dry but laparatomy showed exudate present
Large abscess	1	1			
Cholecystitis with adhesions	1	..	..	1	No fluid obtained; scanty exudate present
Ruptured diverticulum of cecum	1	1			
Total	22	14 64%	3 13%	5 23%	

While a positive result of a tap is of diagnostic value, a negative result should be disregarded, especially in the face of other diagnostic signs; a negative result indicates usually only failure to obtain fluid which is present.

Peritoneal tap should be reserved for a selected group of cases presenting confusion in diagnosis, and the interpretation of the smear must be painstaking.

In cases in which perforated peptic ulcer is suspected, when diagnostic data are confusing and likely to lead to exploratory laparotomy the recovery by peritoneal tap of methylthionine chloride (methylene blue) previously introduced into the stomach will establish the exact diagnosis.

While the results of the procedure were of definite clinical value in only 62.6 per cent of our 22 cases, the diagnosis in all of these presented great difficulties and could be established accurately only by exploratory laparotomy. The tap in these cases established data that determined diagnosis and aided definitely in treatment as well as in evaluation of prognosis.

ALKALINE AND ACID PHOSPHATASE LEVELS IN THE SERUM OF DOGS AFTER LIGATION OF THE COMMON BILE DUCT

JESSE L. CARR, M.D., AND FREDERICK S. FOOTE, M.D.
SAN FRANCISCO

Use of values of phosphatase activity in the serum as an index of hepatic function was first studied by Roberts,[1] in 1933, who found that there was a marked increase of alkaline phosphatase activity with obstructive jaundice, a slight increase with catarrhal jaundice and no increase with hemolytic jaundice. He stated the belief at this time that, in addition to indicating an increased osteoplastic activity, an increased alkaline serum phosphatase activity might also act as a differential diagnostic measure in some types of hepatic disease.

In 1934 Davies,[2] Bamann and Riedel[3] found that the spleen, kidneys and liver of swine and cattle contained phosphatases which had optimum activities at two ranges of p_H. One of these was at approximately p_H 4.8 and the other at p_H 9 to 9.5.

After the original demonstrations of phosphatases with optimum activities at two ranges of p_H in mammalian tissue, interest in phosphatases became centered on cases of malignant diseases. No widespread use of values of phosphatase activity, either alkaline or acid, has been made in the differential diagnosis of hepatic disease, and in order to study this problem and to elucidate further the activity of phosphatases of both alkaline and acid type the following experiment is presented.

Ten dogs were selected from a routine stock, quarantined for two weeks in steam-heated cages and fed the stock laboratory diet utilized at the University of California Medical School; after the two week quarantine the common bile ducts were ligated, with the animals under ether anesthesia. On the day before surgical operation an initial determination of the acid and alkaline phosphatase levels of the serum was made by the method of King and Armstrong on blood withdrawn from the femoral vein. The initial level of alkaline phosphatase for these animals was found to range from 4 to 9 units and that of the acid phosphatase from 1 to 11 units. Four of the animals died within a week after operation, and, while one determination of the phosphatase level was obtained for each of them, they were discarded from the series as inadequate material.

The remaining 6 dogs lived from five to fourteen weeks after operation, their phosphatase levels being computed at weekly intervals during the postoperative survival period. Within the first week after obstruction of the common ducts by surgical ligation the alkaline phosphatase levels were found to rise to between 70 and 90 units while the acid phosphatase levels remained at between 2 to 4 units.

After the first week the phosphatase levels either rose gradually or remained essentially the same during the remainder of the survival time, with minor fluctuations, which may be attributed to variations in biochemical technic and fluctuations in photoelectric activity of the colorimeter.

At the end of four weeks a cholecystoduodenostomy was done on 2 animals. For 1 of these the phosphatase level, which had already dropped somewhat the third week, progressed at this time gradually downward until it became normal five weeks later, or nine weeks after the initial ligation of the common duct. For the other animal, the phosphatase level rose abruptly after operation for a short period, after which it dropped. It also was normal nine weeks after the initial ligation, or five weeks after the reestablishment of the flow of bile through the gallbladder into the duodenum.

Unfortunately no other concomitant tests of hepatic function were done on these animals except the cephalin-cholesterol precipitation test of Hangar, which within a short time after the initiation of the experiment was found to be unsuitable for dogs.

The degree of alkaline phosphatase activity was much greater than could be accounted for by

From the departments of Pathology and Surgery, University of California Medical School.

1. Roberts, W. M.: Blood Phosphatase and van den Bergh Reaction in Differentiation of Several Types of Jaundice, Brit. M. J. **1**:734-738, 1933.

2. Davies, D. R.: Phosphatase Activity of Spleen Extracts, Biochem. J. **28**:529-536, 1934.

3. Bamann, E., and Riedel, E.: Ueber das Vorkommen zweier durch das p_H Wirkungsoptimum unterscheidbaren Phosphoesterasen in tierischen Organen, Ztschr. f. physiol. Chem. **229**:125-150, 1934.

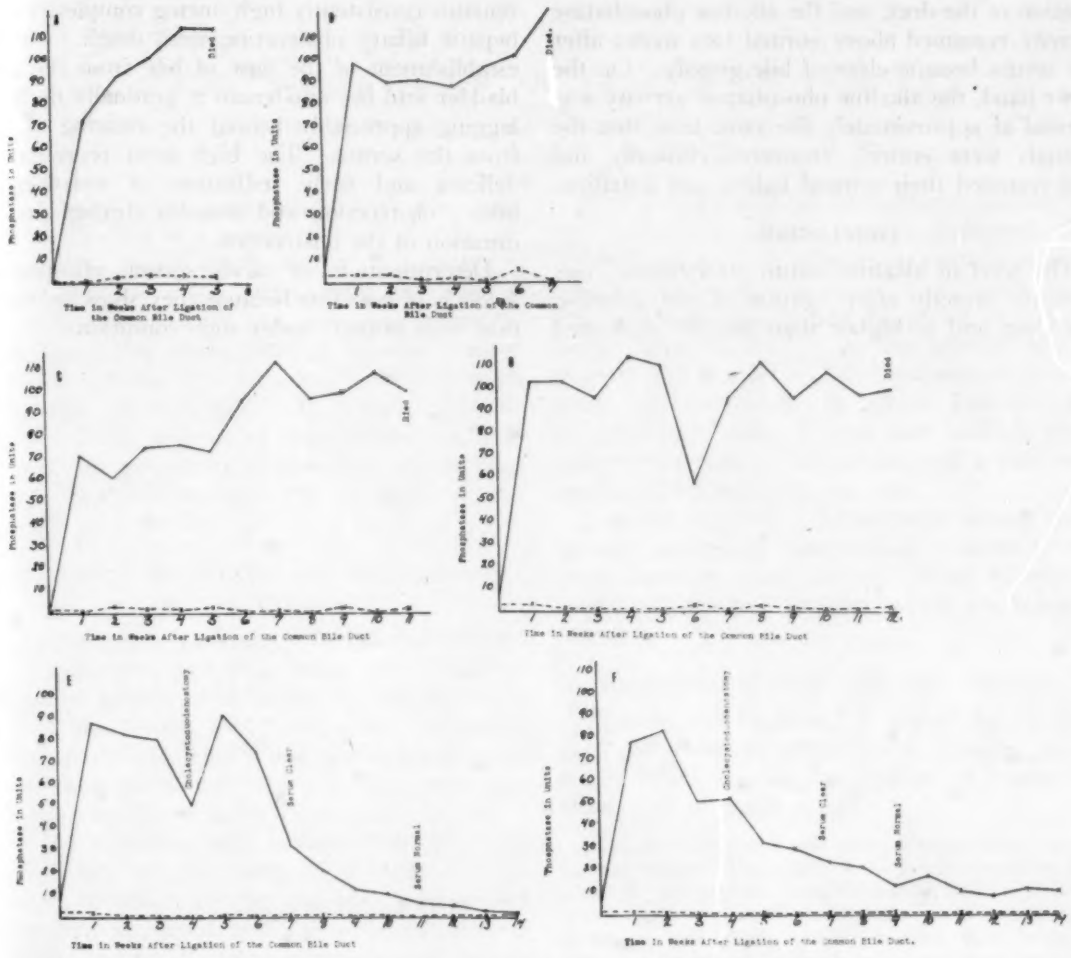

Chart 1.—*A*, serum phosphatase levels for dog 360. *B*, serum phosphatase levels for dog 404. *C*, serum phosphatase levels for dog 414. *D*, serum phosphatase levels for dog 402. *E*, serum phosphatase levels for dog 398. *F*, serum phosphatase levels for dog 407. The solid line represents the alkaline phosphatase level. The line of short dashes represents the acid phosphatase level.

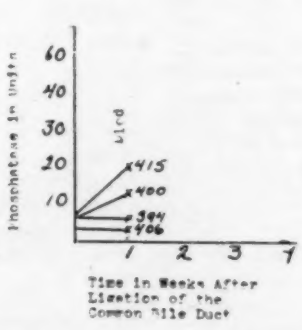

Chart 2.—Serum phosphatase levels for dogs 415, 400, 394 and 406. The solid line represents the alkaline phosphatase level.

the amount of bile observed in the serum after ligation of the duct, and the alkaline phosphatase activity remained above normal two weeks after the serum became clear of bile grossly. On the other hand, the alkaline phosphatase activity was normal at approximately the same time that the animals were entirely recovered clinically and had resumed their normal habits and nutrition.

CONCLUSION

The level of alkaline serum phosphatase rises abruptly directly after ligation of the common bile duct and is higher than can be accounted for by the amount of bile in the blood. It remains consistently high during complete extrahepatic biliary obstruction until death. On reestablishment of the flow of bile from the gallbladder into the duodenum it gradually declines, lagging appreciably behind the clearing of bile from the serum. The high level represents a delicate and early indication of extrahepatic biliary obstruction and remains throughout the duration of the obstruction.

Determination of acid serum phosphatase levels is of no value because they show no variation from normal under such conditions.

LOCAL IMPLANTATION OF GELATIN IN WOUNDS

J. A. SINCLAIR, D.D.S., AND BEVERLY DOUGLAS, M.D.
ASHEVILLE, N. C. NASHVILLE, TENN.

This work was undertaken with the idea that the healing of a wound through fibroplasia might take place more readily if substances needed by the cells surrounding the wound were supplied locally in adequate amounts throughout the entire healing process, rather than if the body were left alone to supply such substances more slowly. By local implantations in fresh wounds of normal persons, this form of therapy seeks to speed up the healing process and to increase the strength of the wounds so treated.

THE EFFECT OF GELATIN ON THE HEALING OF THE WOUNDS

In emergency operations for dental extraction during the past two years, one of us has implanted gelatin in all operative wounds, with results that seem to justify the treatment. Equal parts of gelatin and sulfanilamide are mixed into the blood before it clots, and usually the wound is closed with sutures.

In the beginning only sulfanilamide was used on one side of the mouth as a control. The wounds in which gelatin was also used healed faster and appeared healthier than the control wounds, and no ill effects were observed in any of them. More than 100 wounds have been treated with implantations of gelatin and sulfanilamide.

The healing effect of gelatin may be attributed to the excess of preformed collagen provided or to the excess of the essential amino acids which it supplies. The following statements by Lund and Crandon [1] in their discussion of "Nutrition As It Affects Wound Healing" seem to substantiate these assumptions:

> The symptoms, signs and gross pathology of scurvy have been long understood. However, the fact that intercellular collagen could not be formed in the scorbutic state is comparatively recent knowledge. Although ascorbic acid has an important intracellular function as an enzyme effective in oxidation-reduction systems, it is the failure of deposition of collagen in its absence that causes failure of healing.

At the beginning of the present studies we felt that since clinical results indicated that the implantation of gelatin in wounds seemed valuable in promoting more rapid and more stable healing this should be tested in experimental wounds, both in normal animals and in animals reduced by dietary measures to a partially scorbutic state, in which Lanman and Ingalls [2] have demonstrated that wounds show "defective repair of the corium, and a poor production of collagen in the scar."

Dogs were found to be included among those animals capable of synthesizing vitamin C and were therefore used in our series of experiments on "normal" animals, which are reported herewith.

PROPERTIES OF COLLAGEN AND GELATIN

Harrow and Sherwin,[3] in describing the physical and chemical properties of collagen, which is the main organic constituent of connective tissue and of bone, stated:

> Collagen is found in the white fibrous tissue beneath the epidermis. The tissue is in bundles separated by a sort of sarcolemma. Interstitial cells, blood vessels and lymph spaces separate the bundles from one another. The size and shape of the bundles vary with the location. In the skin, the bundles are short and thick and cause the "pebbling" of the surface of the skin; while in tendons, the bundles are long and attenuated. . . .
>
> The intimate structure of the collagen bundle is not clear. Probably, it involves a fibrous structure, the fibers being bound into bundles by means of "hulls," connective-tissue cells something like those that surround the nerve fibers. When collagen is converted into gelatin these "hulls" are torn and the fibers are free. . . .
>
> Collagen is digested by pepsin-hydrochloric acid to polypeptides, but it is affected by trypsin only at temperatures above 40 C. The tissue "autolytic" enzymes do not hydrolyze collagen at body temperature. . . .
>
> Gelatin is produced when collagen is boiled for a time in distilled water. The time necessary to convert collagen into gelatin varies with the kind of collagen. . . .

The authors then stated that a longer time of boiling is required to convert collagen de-

From the Department of Surgery, Vanderbilt University School of Medicine and the office of Dr. J. A. Sinclair.

1. Lund, C. C., and Crandon, J. H.: Nutrition as It Affects Wound Healing, M. Clin. North America **27**: 561-563 (March) 1943.

2. Lanman, T. H., and Ingalls, T. H.: Vitamin C Deficiency and Wound Healing, Ann. Surg. **105**:616-625 (April) 1937.

3. Harrow, B., and Sherwin, C. P.: A Textbook of Biochemistry, Philadelphia, W. B. Saunders Company, 1935, p. 694.

rived from the skin into gelatin than that required to convert collagen from the achilles tendon into gelatin and continued as follows:

The prevalent view seems to be that conversion of collagen to gelatin involves only a physical change. There is no increase in amino nitrogen, as one would expect if a chemical change, like hydrolysis, were involved. X-ray diagrams of air-dried collagen and air-dried gelatin are identical (d = 4.5 Å). . . .

The chemical composition of collagen is rather the chemistry of gelatin which is produced from it when collagen is boiled. The analyses of Dakin are the most complete. In addition we give data from other sources.

Then followed the table which is reproduced below.

Amino acid	Per cent	Amino acid	Per cent
Aminoacetic acid	25.5	Tyrosine	.00
Alanine	8.7	Proline	9.5
Valine	.0	Hydroxyproline	14.10
Leucine	7.1	Tryptophan	.00
Serine	.4	Histidine	.9
Aspartic acid	3.4	Arginine	8.2
Glutamic acid	5.8	Lysine	5.9
Cystine	.0	Methionine	.97
Phenylalanine	1.4		

An essential amino acid, according to Duncan,[4] is an amino acid which cannot be synthesized by the body but must be supplied in the diet. He listed the essential or indispensable amino acids, in the order of their importance with respect to growth, as lysine, tryptophan, histidine, phenylalanine, leucine, isoleucine, threonine, methionine, valine and arginine. Arginine can be synthesized by the animal organism, but not at a sufficiently rapid rate to meet the demands of normal growth, the author stated.

It will be noted that all the essential amino acids except tryptophan, valine and threonine are in the preceding analysis of gelatin. Harrow[5] quoted Williams' recent analysis of gelatin, which shows that it contains threonine (1.4 per cent).

Gelatin has been employed subcutaneously to arrest internal hemorrhage and to cause coagulation in sacculated aneurysms.

Gelatin[6] has been used most frequently in our experiments, although collagen and ossein have also been employed in a certain number.

EXPERIMENTAL WORK

Since June 1942 experiments with implantations in wounds have been carried out in the department of surgery at Vanderbilt University. They were of two main types: In series I wounds of equal length were made vertically on the backs of dogs in the middorsal region and later separately excised. In series II similar wounds were made but were arranged parallel to each other on opposite sides of the spine, so that a transverse strip of skin of measured constant width including both could be excised later.

Since, with minor modification, all experiments were identical, the following actual description of one may be considered as typical of all.

Fig. 1.—Photograph showing a critical test of the tensile strength, by weight, of two wounds simultaneously. The upper or control wound ruptured before the lower or gelatin-treated wound. The strips of skin were the same width at the sites of the wounds. (Photograph by Tommy S. Gibson.)

EXPERIMENT.—Dog 302 was anesthetized with pentobarbital sodium. The entire back was shaved from the midscapular to the sacral region. The skin was prepared with iodine and alcohol. With a sterile technic three wounds measuring 5 cm. in length and approximately 7 mm. deep were made vertically with a scalpel through the skin, the subcutaneous tissue and the superficial fascia. Two of these wounds were placed one above the other in the middorsal region to the left and to the right of the spine respectively. After control of bleeding, by pressure and by ligatures of black silk around a few vessels, collagen was dusted on the edges of one wound and gelatin on a second, while nothing was applied to the third or control wound. The three

4. Duncan, G. G.: Diseases of Metabolism, Philadelphia, W. B. Saunders Company, 1942, p. 80.

5. Harrow, B.: A Textbook of Biochemistry, ed. 3, Philadelphia, W. B. Saunders Company, 1943, p. 53.

6. The gelatin used in both our experimental and our clinical work was prepared under the direction of D. Tourtellotte, director of research, Knox Gelatine Company, Johnstown, N. Y.

wounds were then closed with interrupted fine silk sutures, through the skin and the subcutaneous tissues. As far as possible the same number of sutures was used in each. The dressings consisted of dry gauze over the wounds and a binder of elastoplast as a girdle applied with moderate pressure around the trunk. This binder served to prevent soiling.

The wounds were inspected at seventy-two hours, and more inflammation, evidenced by more reddening and moisture, was present in the control lesion than in either of the other two wounds.

Fig. 2.—Photograph showing vertical sutured wounds on a dog's back. Two wounds on the left, in which gelatin was implanted seven days before, healed with less exudation and had greater tensile strength than the untreated control wounds on the right. (Photograph by T. S. G.)

One week after the operation the skin and subcutaneous tissue containing each wound were excised to equal widths by elliptic incisions, care being taken to avoid tension on the sutures during removal. The stitches were then removed, and one through and through suture of silk was passed on opposite sides of the healing wounds at a distance of 1 cm. from each. By attaching one of these sutures to an ordinary ring stand and the other to a scale pan (fig. 1) and adding weights to the pan, we accurately determined the relative tension required to rupture each of the wounds.

Result.—The tension, by weight, required to rupture the wounds excised seven days after operation was 750 Gm. for the wound in which gelatin was implanted and 370 Gm. for the control wound. In several of the wounds collagen and ossein (prepared by the Knox Gelatine Company) were substituted for gelatin. While these substances also increased the strength of the wounds, the gelatin proved definitely superior in this respect. It is thought that this superiority may have been due to the fact that the gelatin used had more finely ground particles and was more soluble in the wound than the collagen or the ossein.

The main difference in the experiments in series II was that the wounds with implantations of gelatin and those without were made parallel and the skin was excised by incisions at right angles to them (figs. 2 and 3). By introducing a suture at each end of the strip lateral to each wound, tension could be exerted equally through the two simultaneously, in order to determine which one would rupture first. In most of these experiments several strips 0.5 cm. wide including both wounds were cut from each larger strip and the point of rupture was determined by a similar technic on each of the smaller strips (fig. 1).

After rupture of one of the wounds a suture was inserted near the ruptured edge, and after resuspension weight was added to the point of rupture of the other.

RESULTS OF EXPERIMENTS

SERIES I.—Up to the time of writing 70 wounds have been made for the experiments in series I. Some wounds were used for histologic studies alone. In rare instances intercurrent infection occurred in both wounds, and in others damage resulted from excision. All of these were discarded.

Results.—The tension, by weight, required to disrupt 14 wounds in which gelatin was implanted was 622.1 Gm.; that required to disrupt untreated control wounds in the same dogs was 411.5 Gm. Thus the wounds frosted with gelatin before being sutured at the end of a week were 33.9 per cent stronger on the average than the control wounds, in which gelatin was omitted.

Actually in some of the experiments the comparative difference in the strengths of the two wounds was much greater. Several of the "gelatinized" wounds were more than twice as strong as their controls, and many others were 50 to 75 per cent stronger.

There is no doubt that, although an abundance of granular gelatin in a wound does not seem to prevent its healing in a stronger way than when it is not applied at all, too much may act as a foreign body for a time. It is felt that when the amount is determined to give the optimum supply of intercellular substance before complete absorption the strength of the healing wound will greatly exceed that of the untreated wound.

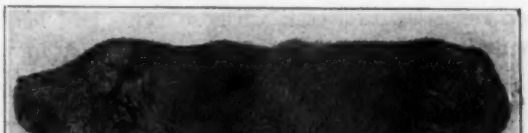

Fig. 3.—Photograph showing an excised strip of skin from the dog's back, as shown in figure 2. Strips of skin of measured width were cut lengthwise from a larger strip for testing the tensile strength. The gelatinized wound at the left showed less reddening of surrounding edges and less exudation than the untreated control wound at the right. (Photograph by T. S. G.)

Of the 14 experiments there were only 2 in which the control wounds were slightly stronger than the treated wounds. In these the differences were less than 16 per cent. They may be regarded as the exceptions which prove the rule.

SERIES II.—In series II there were 10 experiments in which strips of skin containing both the gelatinized wound and the control wound were subjected to increasing tensions by suspending weights on the strips (fig. 1). Technical difficulties, such as formation of a hematoma or tension on the wound during excision, may possibly explain the results in these experiments. In 9 of 10 the control wounds ruptured first, and in 1 the gelatin-treated wound ruptured before the control. In the latter experiment the control wound ruptured at 500 Gm. while the treated wound ruptured at 400 Gm. At the other extreme, 1 control wound ruptured at 550 Gm. while the gelatin-treated wound withstood a pressure of 900 Gm. before rupturing. With this severe and critical test 90 per cent of the gelatin-treated wounds easily withstood tensions which ruptured the control wounds.

Absence of Irritation from Gelatin.—An observation in all of our experiments, which seems significant, was that signs of irritation or reaction of the tissues to implantation of gelatin were entirely absent. In no single experiment did we note irritative phenomena of any kind. In fact, the gelatin-treated wounds appeared to be drier and to heal with less signs of inflammation than nearby control wounds.

Further evidence of the nonirritative properties of gelatin was furnished by our clinical experience with local implantation of dried sterile powdered gelatin in ulcers.

CLINICAL APPLICATION OF GELATIN TO ULCERS ON THE LEG

In order to observe the effect of gelatin on human wounds several ulcers on the leg were selected. In 1 case of recent superficial ulceration on a leg in which varicose veins had been treated, the ulcers were covered with a light layer of finely powdered gelatin and, as usual, elastoplast was wound around the leg so that its adhesive under surface was directly in contact with the gelatin and the wounds. When the bandage was removed, twelve days later, healing was complete and the surrounding skin showed no irritation.

This form of dressing was also tried on 4 deeper ulcers of the leg surrounded by scar tissue. In each case the ulcers had been treated for long periods of time in the outpatient clinic with elastoplast alone directly on the ulcers or with sulfathiazole under the elastoplast. In each case healing had failed to occur.

In 2 of these cases one part of sulfathiazole and three parts of gelatin were used, and in 2 one part of sulfadiazine and three parts of gelatin were used under the elastoplast. Healing occurred in each in a period which must be considered short for deep ulcers.

We feel that by local implantation of gelatin in wounds in scarred areas or in patients with hypoproteinemia or lowered reserves of vitamin C intercellular substances may readily be supplied and therefore fibroplasia may proceed more nearly normally.

Other series of experiments designed to determine the effect of gelatin on wounds of subcutaneous tissues, of fascia and of tendons and on fractures of bone and a separate series on wounds in guinea pigs reduced by dieting to a subscorbutic state are under way.

CONCLUSIONS

Although much of the work on this and related subjects is still in progress, we feel that the following conclusions are justified from results thus far obtained:

1. Implantation of both gelatin and the closely related collagen results in their utilization in experimental sutured wounds in such a way that the strength of these wounds is greatly increased over that of untreated control wounds.

2. Application of gelatin to fresh, open wounds from extractions of teeth and to the soft parts of ulcers appears to hasten the process of fibroplasia and to produce more rapid, stable healing than occurs in similar wounds not so treated.

3. Sulfonamide compounds and gelatin possess no chemical or physiologic incompatibility and have therefore been mixed and implanted advantageously in contaminated wounds.

CAVERNOUS HEMANGIOMA OF THE LUNG (ARTERIOVENOUS FISTULA)

REPORT OF A CASE WITH SUCCESSFUL TREATMENT BY PNEUMONECTOMY

W. E. ADAMS, M.D.; T. F. THORNTON JR., M.D., AND LILLIAN EICHELBERGER, PH.D.

CHICAGO

Cavernous hemangioma of the lung is one of the rarest lesions. The association of this condition with compensatory polycythemia has been reported in only 4 cases in medical history. The case reviewed in this paper was the first in more than 240,000 admissions at the University of Chicago Clinics in the last fifteen years, and more than 4,380 autopsies at the same institution did not reveal another such lesion.

In 1942 Hepburn and Dauphinee [1] reported the first case in which hemangioma of the lung was diagnosed from clinical and laboratory information and in their discussion included a review of the literature. Their case was also the first one reported in which a cure was obtained following total pneumonectomy.[2]

Ten cases of hemangioma of the lung reported in the literature are given in table 1, in 5 of which the hemangiomas may be rated definitely as cavernous (cases 5, 7, 8, 9 and 10). It is significant that the symptoms and the findings are practically identical in all 5 of these cases.

REPORT OF A CASE

R. R., a white man 24 years old, entered the University of Chicago Clinics on Jan. 24, 1943, complaining of frequent nosebleeds and colds over the last two or three years. He also had suffered from generalized cyanosis and clubbing of the fingers and toes for at least sixteen years.

At the age of 6 years the patient had an attack of influenza, soon after which the clubbing of the fingers and the cyanosis were noted. Throughout the past two years he had been inconvenienced by a mildly productive cough, which was aggravated when he was lying on the left side. The man had worked as a farm laborer prior to the past year but had never been incapacitated by his physical condition.

The family history showed that the patient's father had had blue spots on his lips and had been subject to numerous nosebleeds. Roentgenograms of the parent's chest had revealed some shadows. Other male ancestors in the family were reputed to have had nosebleeds and blue spots on their lips.

Physical Examination.—The patient was well developed physically and appeared to be fairly well nourished, although giving the impression of being older than 24. The extreme cyanosis of the lips and the moderate cyanosis of the entire head and neck were pronounced enough to be arresting. The lips had small dark red spots (hemangiomas). Several small hemangiomas were also present on the face. A small ulceration of the nasal mucous membrane was found to be the source of his epistaxis. Otherwise the head and the neck were normal. The fingers and the toes were extremely clubbed and moderately cyanotic. The ankles and the wrists were enlarged and slightly cyanotic. The pulse rate was 70 per minute; the respiratory rate was 16 per minute, and the blood pressure was 110 systolic and 80 diastolic. The temperature was normal. The chest was symmetric, with little abnormality on percussion or auscultation. For a thin person the respiratory sounds were diminished throughout. The heart was normal in size and position, and the tones were normal. Examination of the abdomen, the genitalia and the rectum revealed normal conditions. The extremities had normal strength and range of motion. Sensation and reflexes were intact. The patient was cooperative and of average intelligence. He was definitely concerned about his condition but had become reconciled to the hopelessness of the prospects of improving it.

Laboratory Findings.—1. The red blood cells numbered 7,200,000 per cubic millimeter and the white blood cells 6,600, and the hemoglobin content was 23 Gm. per hundred cubic centimeters. The total blood volume was 12,750 cc., of which the plasma volume was 2,420 cc. and the cell volume 10,330 cc.[3] 2. The urine was normal. 3. The vital capacity of the lungs was 3,800 cc. 4. Roentgenograms of the chest showed a lobulated, moderately opaque area covering about 25 sq. cm. located between the left seventh and ninth ribs posteriorly. A second similar opacity, 1 cm. in diameter, was seen in the midaxillary line at the level of the right sixth rib. Roentgenograms of the extremities revealed the formation of considerable periosteal new bone from the bones of the forearm and leg distalward.

From the preceding data three conditions were considered in the differential diagnosis: (1) pulmonary fibrosis; (2) arteriovenous shunt in the lung (in view of the circumscribed lesions of the lungs a shunt through an arteriovenous aneurysm seemed most likely; the poly-

From the Departments of Surgery and Medicine of the University of Chicago.

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1. Hepburn, J., and Dauphinee, J. A.: Successful Removal of Hemangioma of Lung Followed by Disappearance of Polycythemia, Am. J. M. Sc. **204**:681, 1942.

2. Shenstone, N. S.: Cavernous Angioma, in Medical-Surgical Tributes to Harold Brunn, Berkeley, Calif., University of California Press, 1942, pp. 503-507.

3. Schafer, P. W.: A Simplified Dye Dilution Method for Determining Plasma Volume, unpublished work.

cythemia was thought to be secondary); (3) congenital cardiac disease.

The patient was admitted to the hospital for further study.

Bronchoscopy showed the mucous membrane of the larynx, trachea and bronchi to be dull red and chronically congested. A moderate amount of tenacious secretion was removed. An electrocardiogram was normal.

The oxygen content of the venous blood was 22.48 volumes per cent and the oxygen capacity 34.5 volumes per cent. The oxygen content of the arterial blood was 25.08 volumes per cent and the oxygen capacity 35.5 volumes per cent. Therefore, the proportion of hemoglobin oxygenated in the venous blood was 65 per cent and in the arterial blood 71 per cent.

Other analyses are shown in table 2.

In view of these findings an arteriovenous shunt, chiefly in the left lung, was thought quite likely, and the patient was prepared for an exploratory operation by the removal of 700 cc. of blood by venesection.

TABLE 1.—*Hemangioma of the Lung* *

Author	Age	Sex	Complaints	Physical Findings	Blood	Outcome
1. de Lange, C., and de Vries Robles, S. B.: Ztschr. f. Kinderh. **34**: 304, 1923	2.5 mo.	..	None related to lungs	Autopsy—two pulmonary tumors; capillary hemangioma	Unknown	Died
2. Wollstein, M.: Arch. Path. **12**: 562 (Oct.) 1931	4 mo.	..	.....	Autopsy—malignant hemangioma	Anemia	Died
3. Hall, E. M.: Am. J. Path. **11**: 343, 1935	40 yr.	F	.....	Malignant hemangioma	Anemia	Unknown
4. Bowers, W. F.: Nebraska M. J. **21**: 55, 1936	2 days	..	Pulmonary hemorrhage	Autopsy—hemangioma of the lung	Unknown	Died from hemorrhage
5. Rodes, C. B.: J. A. M. A. **110**: 1914 (June 4) 1938	25 yr.	M	Dyspnea, cyanosis, pulmonary hemorrhage	Clubbing of fingers and toes, cyanosis, pulmonary opacities	Polycythemia, polyhemoglobinemia	Died from hemorrhage
6. Duvoir, M.; Picot, G.; Pollet, L., and Gaultier, M.: Étude clinique, Bull. et mém. Soc. méd. d. hôp. de Paris **55**: 506, 1939	12 yr.	..	Dyspnea	Pulmonary opacities	Normal	Died of pneumonia
7. Smith and Horton [12]...	47 yr.	M	Cyanosis, dyspnea on exertion, weakness, vertigo, tinnitus	Cyanosis, clubbing of fingers and toes	Polyemia, polycythemia, hyperhemoglobinemia	Unknown
8. Hepburn and Dauphinee [1]	23 yr.	F	Dizziness, dyspnea, clubbing of fingers	Cyanosis, clubbing of fingers, pulmonary opacity	Polyemia, polycythemia, hyperhemoglobinemia	Pneumonectomy, well
9. Goldman, A.: Dis. of Chest **9**: 479, 1943	22 yr.	M	Cyanosis, clubbing of fingers and toes	Cyanosis, clubbing of fingers and toes, pulmonary opacity	Polyemia, polycythemia, hyperhemoglobinemia	Living
10. U. of C. Clinics 1942	24 yr.	M	Epistaxis, cyanosis, clubbing of fingers	Cyanosis, clubbing of fingers and toes, pulmonary opacity	Polyemia, polycythemia, hyperhemoglobinemia	Pneumonectomy, well

* Case reports of hemangioma of the lung. The lesions described in reports 5, 7, 8, 9 and 10 were cavernous and had produced a compensatory polyemia, polycythemia and hyperhemoglobinemia.

TABLE 2.—*Status of the Blood Before and Following Total Pneumonectomy for Cavernous Hemangioma (Arteriovenous Fistula) of the Left Lung*

Date	Therapy and Comments	Red Blood Cells, Millions	Hemoglobin, Gm.	Hematocrit Reading, per Cent	White Blood Cells	Blood Volume
2/ 8/43	Vital capacity 3,800 cc.	7.2	23.0	82	8,500	.....
2/10/43	700 cc. blood removed (venous section)..	....	....	....	.....	Total volume 12,750 Plasma volume 2,430 Cell volume 10,300
2/11/43	Pneumonectomy	....	....	....	.....	.....
2/11/43	600 cc. plasma intrapleurally, 2,400 cc. plasma intravenously	5.05	15.5	62	.....	.....
2/12/43	Blood loss at operation 2,200 cc. +.....	5.10	16.5	63	7,000	.....
2/13/43	300 cc. plasma intrapleurally, 800 cc. plasma intravenously	....	....	61.5	.....	Total volume 6,900 Plasma volume 2,650 Cell volume 4,250
2/15/43	.....	6.04	17.0	51.5	8,700	.....
2/18/43	.....	5.10	15.0	53	9,800	.....
2/20/43	.....	5.12	16.0	....	10,700	.....
2/23/43	.....	....	....	54	.....	Total volume 6,350 Plasma volume 2,920 Cell volume 3,430
2/25/43	.....	4.94	17.0	52	11,700	.....
3/12/43	.....	5.33	17.8	....	12,300	.....
3/26/43	.....	5.42	17.5	....	8,400	.....
4/23/43	Vital capacity 2,200 cc.	5.49	17.7	....	8,600	.....
5/21/43	.....	5.16	16.7	....	7,900	.....
11/22/43	Working	5.05	15.7	54	10,600	Total volume 4,970 Plasma volume 2,280 Cell volume 2,690

Operation.—With the patient under ethylene-oxygen-ether anesthesia (introduced under mild positive pressure through a snug-fitting face piece) the left pleural cavity was entered through the sixth rib bed. The apex of the lower lobe of the left lung posterolaterally was attached to the parietal pleura over an area 4 by 5 cm. by extremely vascular adhesions. Pulsations with each heart beat were visible and palpable on the pulmonary surface covered by the adhesions. This area could be depressed manually and would refill immediately on release of pressure; hence it was obviously an aneurysm. Two smaller lesions with similar characteristics were noted in the upper lobe of the left lung. A pneumonectomy was therefore thought advisable. The left lung was resected, a technic of individual ligation being used. The vessels were doubly ligated with linen, and the bronchus was closed with two rows of chromic catgut sutures, those of the proximal row being of mattress type. After the hilus was dusted with crystals of sulfathiazole, the wall of the chest was closed in layers without drainage. After closure of the pleural cavity air was removed and replaced with 600 cc. of plasma.

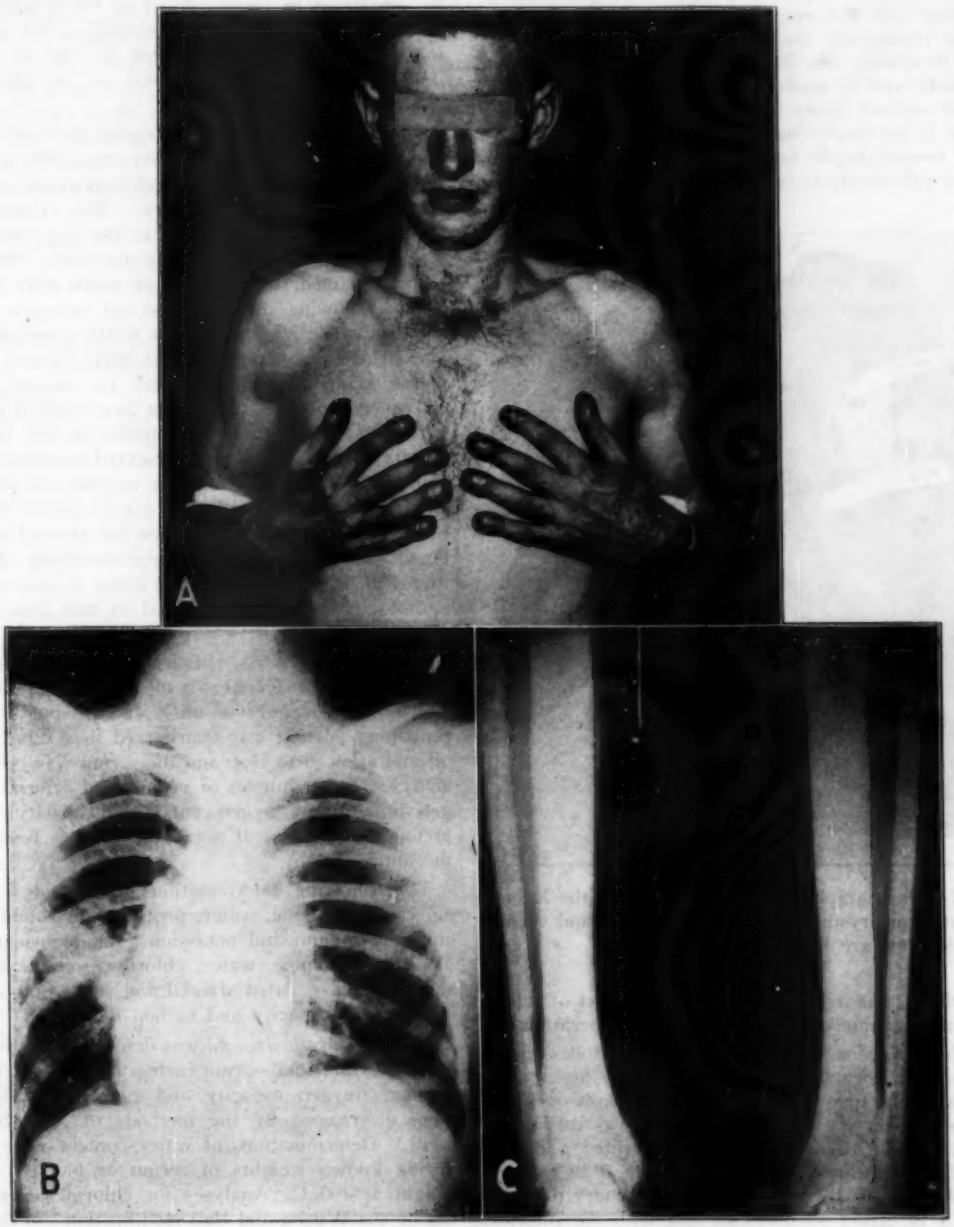

Fig. 1.—*A*, photograph of the patient, showing distinct clubbing of the fingers and cyanosis of the hands and the face. Several small hemangiomas are present on the patient's lips. *B*, roentgenogram of the chest, showing an irregularly shaped circumscribed opacity in the field of the left lung, produced by the hemangioma. An opacity 1 cm. in diameter is barely visible in the third interspace anteriorly near the wall of the chest on the right side. *C*, roentgenogram of the lower extremities, revealing extensive formation of periosteal new bone and sclerosis of the long bones.

The intrapleural pressure was reduced to a normal negative pressure at the end of this procedure.

During the operation the blood which had been lost was partially replaced by 2,400 cc. of plasma given intravenously. This was somewhat less than the 2,200 cc. of blood lost at the operation plus the 700 cc. removed by venesection.

Reaction During Operation.—The blood pressure, the pulse rate and the respiratory rate remained almost constant throughout the operation, the blood pressure being 110 systolic and 70 diastolic at the beginning and 100 systolic and 60 diastolic at the end of the operation, two and one-half hours later. The cyanosis, which was extreme at the beginning of the operation, did not disappear immediately when the pulmonary artery was clamped (as observed by Hepburn and Dauphinee in their patient), but it improved within a period of thirty minutes and continued to do so during the operation.

Fig. 2.—Photograph of the left lung with the largest of the three aneurysms opened. The arterial and venous communications are labeled.

Pathologic Specimen.—On the surface the lobes of the lung appeared normal except for the three areas seen to pulsate at the time of operation. The pleura over the largest of the three (in the lower lobe) was thickened. In a cut section after fixation this presented a multiloculated, smooth-lined cavity, measuring 3 by 4 cm., which communicated with the pulmonary artery through a vessel 4 to 5 mm. in diameter and with the inferior pulmonary vein through a channel 1 cm. in diameter. The two areas in the upper lobe measured 1 to 1.5 cm. in diameter. They were similar to the cavity in the lower lobe but communicated with the lesser circulation through very small vessels. Microscopic sections showed these cavities to be lined by mesothelial cells lying on a fibrous connective tissue wall. There was no hemangiomatous tissue outside of the cavities.

Diagnosis.—Multiple arteriovenous fistulas of the lung.

Postoperative Course.—There were no serious complications following the operation. Administration of sulfathiazole was begun the day before operation. Administration of sulfathiazole and digilanid was continued for seven and fifteen days respectively following the operation. Intranasal inhalation of oxygen (8 to 10 liters per minute) was used for the first few days. The patient's temperature was elevated to 100 to 101 F. for one week, after which it returned to normal. The patient experienced some difficulty with mucus but was relieved by inhalation of steam. Most of the remaining air in the left pleural space was removed on the day following the operation and replaced by 300 cc. of plasma. The patient also received 800 cc. of plasma intravenously.

Immediately after the operation the red cell count and the hemoglobin content were markedly altered (red blood cells fell to 5,000,500 and hemoglobin to 15.5 Gm. per hundred cubic centimeters). The values fluctuated during the subsequent seven to ten days but remained within relatively normal limits thereafter. The patient's color remained somewhat of an ashen gray for several weeks following the operation but has now (one year postoperatively) become more nearly normal. He was discharged from the hospital three weeks after the operation and returned to work two months later. At infrequent intervals the patient has returned to the outclinic for examination and studies on his blood. The results of these studies are presented in tables 2, 3 and 4. Tables 3 and 4 present data on the concentration of electrolytes, water and proteins in serum and whole blood and the values of oxygen for arterial and venous blood before and following pneumonectomy. These findings will be given in detail in order to characterize the pathologic physiology produced by this type of pulmonary lesion.

Venous blood was withdrawn without stasis. One portion was transferred to a tube containing oil, in which it was defibrinated for analyses of whole blood; the remaining portion was transferred to a tube containing oil and allowed to clot, and the serum was removed and analyzed. The samples of venous and arterial blood for determination of oxygen content and capacity were taken in tonometers, neutral potassium oxalate being used as the anticoagulant.

The following determinations were made: on serum, p_H, carbon dioxide, water, protein, nonprotein nitrogen, chloride, sodium and potassium; on defibrinated whole blood, cell volume, water, chloride, sodium and potassium and on oxalated arterial and venous blood, oxygen content and capacity and carbon dioxide.

Chemical Methods.—p_H was determined with the glass electrode, and total serum carbon dioxide, blood oxygen content, oxygen capacity and carbon dioxide content were determined by the methods of Van Slyke and Neill.[4] Determinations of water content were made by drying known weights of serum or blood to constant weight at 100 C. Analyses for chlorides were carried out by the Wilson and Ball modification[5] of the method of Van Slyke.[6] Sodium was determined by the Butler-

4. Van Slyke, D. D., and Neill, J. M.: Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement, J. Biol. Chem. **61**:523, 1924.

5. Wilson, D. W., and Ball, E. G.: Study of Estimation of Chloride in Blood and Serum, J. Biol. Chem. **79**:221, 1924.

6. Van Slyke, D. D.: Determination of Chlorides in Blood and Tissues, J. Biol. Chem. **58**:523, 1923-1924.

Tuthill method[7] and potassium by the method of Shohl and Bennett.[8] The proteins were determined by the micro-Kjeldahl method of Campbell and Hanna,[9] distillation of the ammonia being carried out in the Goebel modification of the micro-Kjeldahl distillation apparatus. The proteins were estimated by multiplying by 6.25 the total nitrogen corrected for the nonprotein nitrogen.

Tables 3 and 4 give the analytic and derived data on the blood before the operation and at intervals following the removal of the lung. It will be noted that the condition of the blood previous to the removal of the lung must be the result of an anoxia brought about by a malformation of blood vessels, causing a large proportion of blood to be shunted from the right to the left side of the heart without being oxygenated.

ciation of oxyhemoglobin. It will be noted that the p_H of the serum and the total carbon dioxide content before operation were 7.42 and 22.86 millimols per liter, respectively. This represents a carbon dioxide tension of 34 mm. of mercury, calculated by the Henderson-Hasselbach equation. This slight alkalosis may cause the kidneys, in their effort to maintain an acid-base balance, to secrete more sodium. For this reason the concentration of sodium in the serum was 133.8 millimols per liter, which is slightly lower than the value found in normal subjects (135 to 138 millimols). These values for sodium and chloride agree with those previously reported by Armstrong and Heim,[10] who stated that anoxic anoxia had little effect on the amount of sodium chloride in the blood. The values for potassium

TABLE 3.—*Concentrations of Electrolytes, Water and Proteins in Serum and Whole Blood Analytic and Derived Data*

		p_H	CO_2, mEq. per L.	Cl, mEq. per L.	Na, mEq. per L.	K, mEq. per L.	H_2O, per Cent	Volume, per Cent	Total Protein, per Cent
Before operation									
2/10/43	Serum	7.42	22.86	97.1	133.8	4.67	93.73	17.8	6.82
	Blood	....	18.32	55.9	32.8	71.8	75.85	82.2	....
	Cells (derived)	....	.....	46.9	10.8	86.4	71.41	....	....
After operation									
2/19/43	Serum	....	32.10	90.5	.....	4.62	94.06	53.2	6.12
	Blood	....	25.85	68.8	.....	....	81.26	46.8	....
4/ 2/43	Serum	....	.....	101.4	140.7	5.00	92.28	61.0	7.52
	Blood	....	21.50	.....	.....	....	.....	39.0	....
5/21/43	Serum	7.43	26.92	102.3	134.8	4.84	92.53	49.5	6.72
	Blood	....	.....	76.2	69.3	54.2	81.60	50.5	....
	Cells (derived)	....	.....	50.5	- 6.13	110.1	70.9	....	....
11/21/43	Serum	7.48	26.60	100.2	137.3	4.46	92.83	39.9	7.55
	Blood	....	20.86	72.8	60.0	58.0	80.53	69.1	....
	Cells (derived)	....	.....	54.5	8.66	93.6	72.5	....	....

TABLE 4.—*Values of Oxygen for Arterial and Venous Blood*

Date		Arterial			O_2 Lost by Blood in Perfusing the Tissues, Vol. per Cent	Venous		
	O_2 Capacity, Vol. per Cent	O_2 Content, Vol. per Cent	Proportion of Hemoglobin Oxygenated, per Cent	O_2 Tension, Mm.*		O_2 Content, Vol. per Cent	Proportion of Hemoglobin Oxygenated, per Cent	O_2 Tension, Mm.*
Before operation								
2/10/43	35.54	25.10	71	37	2.80	22.30	63	32
After operation								
2/14/43	24.70	17.87	72	38	8.60	8.18	33	18
4/ 2/43	22.55	19.85	88	58	8.93	10.92	48	25
5/21/43	22.31	19.46	87	55	....	.....	..	..
11/22/43	24.62	20.86	85	48	7.54	13.32	54	26
Normal blood	20.00	19.00	95	80	4.2	14.80	74	41

* Peters, J. P., and Van Slyke, D. D.: Quantitative Chemical Chemistry, Baltimore, Williams & Wilkins, 1932, vol. 2, p. 527.

Analyses of Serum.—Analyses of the serum before the operation showed that this type of anoxia produced a slight alkalosis, which in turn influenced slightly the concentration of sodium in the serum. The acid-base balance is important in anoxia, since changes in this balance affect the respiratory center and also the dissowere within normal limits, contrary to the values of McQuarrie and his co-workers,[11] who demonstrated that dogs which had been allowed to breathe a 5 to 9 per cent oxygen mixture for a few hours showed a decrease in the serum potassium. Since the period of anoxia of the dog was so brief and the anoxic state of the patient had existed for many years, it is likely that the two results are not comparable.

7. Butler, A. M., and Tuthill, E.: Application of Uranyl Zinc Acetate Method for Determination of Sodium in Biological Material, J. Biol. Chem. **93**:171, 1931.

8. Shohl, A. T., and Bennett, H. B.: A Micro Method for Determination of Potassium as Iodoplatinate, J. Biol. Chem. **78**:643, 1928.

9. Campbell, W. R., and Hanna, M. I.: Determination of Nitrogen by Modified Kjeldahl Methods, J. Biol. Chem. **119**:1, 1937.

10. Armstrong, H. G.: Principles and Practice of Aviation Medicine, Baltimore, Williams & Wilkins Company, 1939, p. 289.

11. McQuarrie, I.; Ziegler, M. R.; Stone, W. E.; Wangensteen, O. H., and Dennis, C.: Studies on Mechanism of Insulin Convulsions: Effects of Varying Partial Pressures of Atmospheric Oxygen and Carbon Dioxide in Adrenalectomized Animals, Chinese M. J. **58**:26, 1940.

It is important that the water content and the concentrations of protein in the serum were normal before as well as following removal of the lung.

Three months following removal of the lung the p_H of the serum was 7.43 and the total carbon dioxide content was 26.92 millimols per liter, which gave a normal carbon dioxide tension, of 41 mm. of mercury. Also, all other determined constituents were normal in value (table 3).

Analyses of Blood.—At normal atmospheric pressure of 760 mm. of mercury, oxygen exerts a partial pressure of 159 mm. At this partial pressure of oxygen the hemoglobin in the arterial blood is 95 per cent saturated with oxygen, or by chemical analyses it contains 19 volumes per cent of oxygen. As the blood passes through the capillary bed, approximately 5 volumes per cent of oxygen is taken by the tissue and approximately 14 volumes per cent of oxygen or hemoglobin oxygenated 70 per cent is left in the venous blood. The dissociation curve of oxyhemoglobin from Barcroft's researches shows that 90 per cent oxygen saturation corresponds to an oxygen tension of 40 mm. of mercury. It will be noted from table 4 that the amount of oxygen present in the arterial blood of this

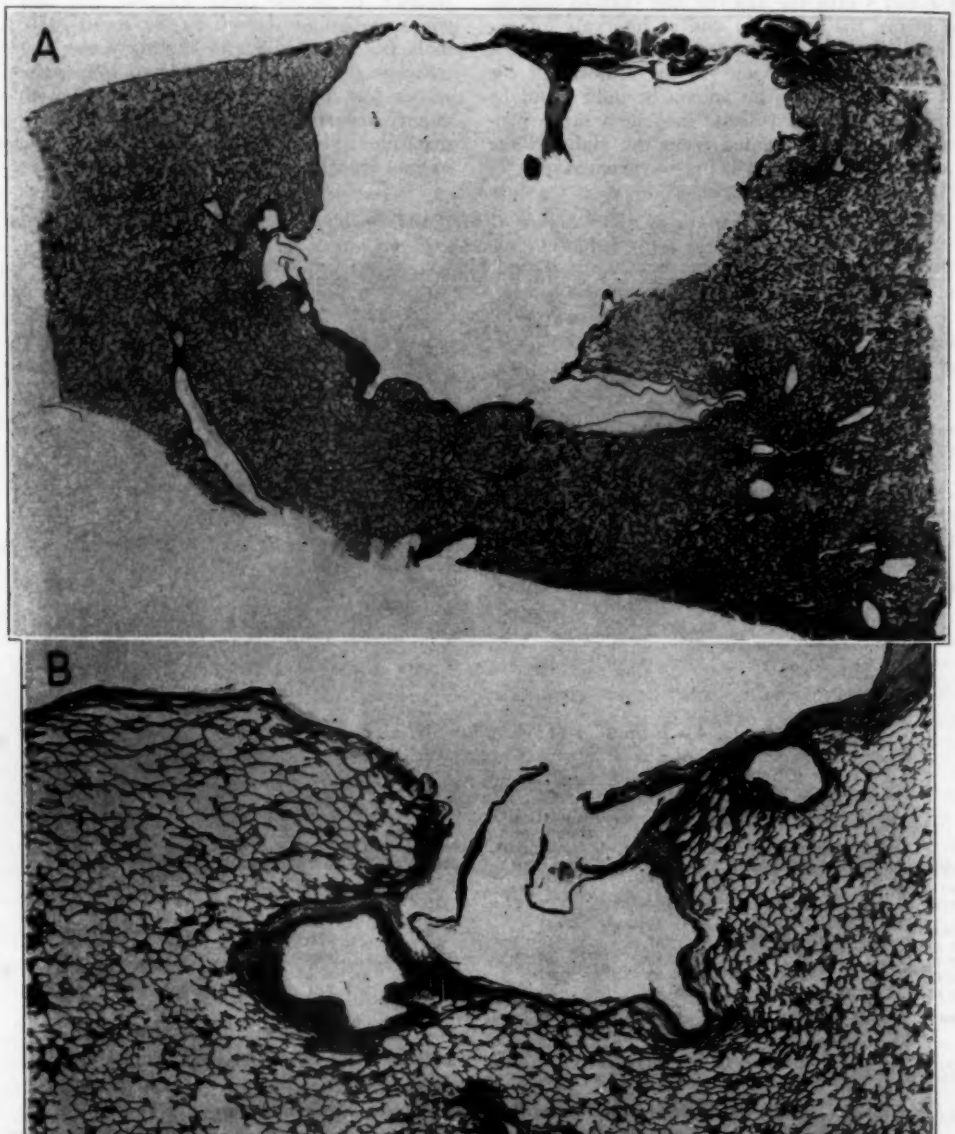

Fig. 3.—Photomicrographs of largest aneurysm of two magnifications. The wall of the aneurysm contains considerable connective tissue, and the space is lined by mesothelium. The adjacent pulmonary tissue is normal.

subject was greater by 5 volumes per cent than that found in normal persons. The reason for this is the determined abnormally large cell volume, of 82 per cent. This is important, but it is more important for the oxygenation of hemoglobin that the oxygen be supplied at a definite pressure.

Before operation, in the arterial blood the oxygen tension was 37 mm. of mercury and the proportion of hemoglobin oxygenated was 71 per cent; in the venous blood the proportion of hemoglobin oxygenated was 63 per cent and the oxygen tension was 32 mm. of mercury. Following the removal of the lung, the proportion of hemoglobin oxygenated in the arterial blood mounted to 85 to 88 per cent and the oxygen tension was 60 mm. of mercury; in the venous blood the proportion of hemoglobin oxygenated fell to 48 to 54 per cent, with an oxygen tension of 26 mm. of mercury.

Normally the oxygen is carried to the tissues at a relatively high pressure, so that there is a considerable gradient of pressure between the blood capillaries and the tissues. If this gradient of pressure is reduced, the tissues are not supplied adequately with oxygen and the rate of oxidation in the tissues is diminished. In our patient before operation this was true. After removal of the lung, the arterial oxygen tension was increased 20 mm. of mercury, causing an increased gradient of pressure between the blood capillaries and the tissues, which resulted in more oxygen being lost to the tissues.

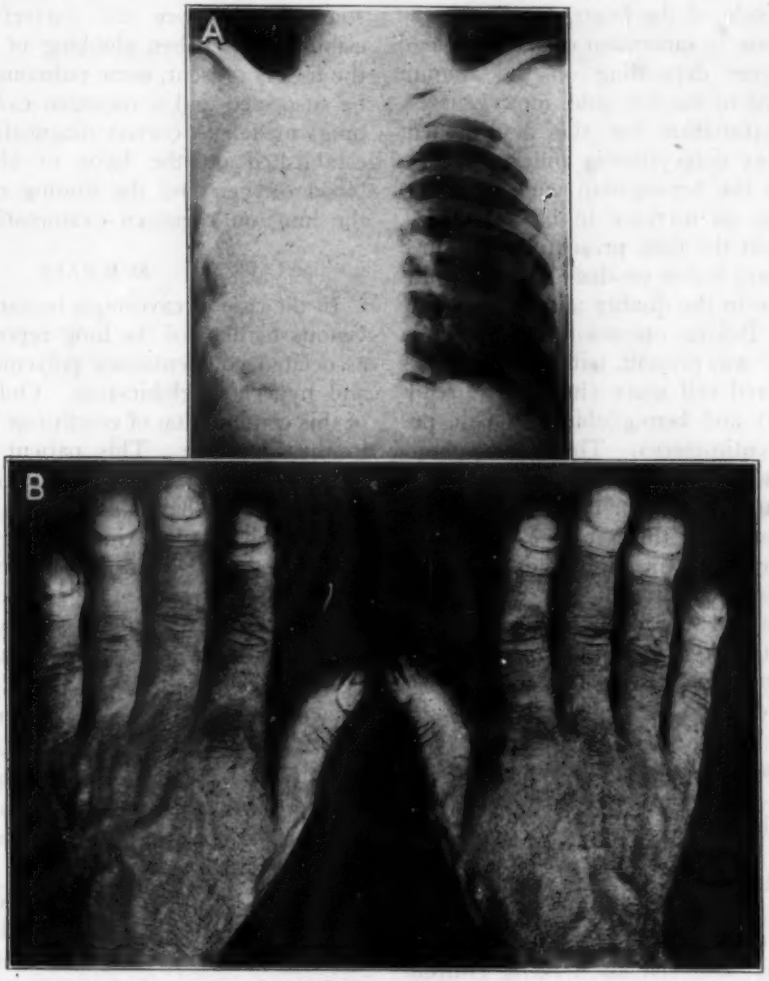

Fig. 4.—*A*, roentgenogram of the chest taken after total removal of the left lung. The left pleural space is entirely filled with plasma. *B*, photograph of the patient's hands approximately five and one-half months following pneumonectomy of the left lung. Note the dark transverse lines across the nails of the fingers and thumb. These lines have moved distalward after the excision of the lung and probably represent metabolic changes produced by its removal.

COMMENT

Most authors who have reported cases similar to the one here presented have described the lesion as a cavernous hemangioma. A careful study of the microscopic sections made from the specimen removed from our patient reveals only normal pulmonary tissue surrounding the three separate mesothelium-lined cavities found in the left lung. On the basis of the pathologic picture, the lesions are really arteriovenous aneurysms or fistulas. It is possible that owing to the

increased pressure, the hemangiomatous tissue may have been broken down and obscured by the connective tissue in the wall of the cavities. The case reported by Smith and Horton [12] suggested that this course of events might have occurred simultaneously with the increase in size of the communication between the pulmonary artery and vein. With a shunting of blood from the right side of the heart directly to the left side a decrease in saturation of arterial blood occurs, the degree depending on the amount of blood returned to the left side unoxygenated. This is the explanation for the development of a compensatory polycythemia and a considerable increase in the hemoglobin content of the blood as well as an increase in blood volume. It is evident from the data presented in table 2 that the pulmonary lesion produced a great compensatory change in the quality and the quantity of the blood. Before operation polycythemia (7,200,000 cells) was present, with a corresponding increase in red cell mass (hematocrit reading 82 per cent) and hemoglobin (23 Gm. per hundred cubic centimeters). The blood volume was approximately two times the normal amount, the increase being entirely in the red cell mass.

After the removal of the left lung, all of the blood was diverted to the right side and was aerated as it passed through the right lung. Immediately the red cell count fell more than 2,000,000 within two days and has remained at a high normal level. This rapid fall was the result of a dilution of the blood caused by the replacement of the blood lost during operation with plasma. The hemoglobin content was reduced from a preoperative level of 23.0 Gm. to the present level of 15.7 Gm. per hundred cubic centimeters. The hematocrit reading was likewise reduced from 82 to 54 per cent. The estimated total blood volume fell from 12,750 cc. (preoperative) to 6,900 cc. by the second postoperative day, this reduction being entirely in the erythrocytes. Ten days later the blood volume was 6,350 cc., a value which is approximately normal; a later determination gave a slightly lower value.

Although only 4 similar cases have been previously reported, the condition in others has likely gone undiagnosed and been treated as polycythemia vera. In 2 of the 4 reported cases the patient was treated for this condition for some time before the correct diagnosis was established. When clubbing of the fingers and the toes is present, some pulmonary lesion should be suspected and a roentgen examination of the lungs made. A correct diagnosis may be readily established on the basis of altered values of blood oxygen and the finding of an opacity in the lung on roentgen examination.

SUMMARY

In the case of cavernous hemangioma (arteriovenous fistula) of the lung reported, there were associated compensatory polyemia, polycythemia and hyperhemoglobinemia. Only 4 other cases of this combination of conditions have been found in the literature. This patient sought medical treatment for repeated epistaxis and extreme cyanosis of the hands and face. On examination he also presented distinct clubbing of the fingers and toes and evidence of pulmonary osteoarthropathy. A roentgenogram of the chest revealed a large, irregularly shaped, circumscribed opacity in the left lung and a small one in the right lung. The arterial blood had an oxygen capacity of 35.54 volumes per cent but contained only 25.10 volumes per cent. Thus only 71 per cent of the hemoglobin was oxygenated.

After removal of the left lung the status of the blood approached the normal one, and the patient returned to work.

Most of the clinical features observed in our patient have been present in the 4 previously reported patients having this condition. In view of the uniformity of the clinical picture a diagnosis can readily be made when the lesion is suspected.

Dr. Paul Schafer made studies on the blood volume of this patient.

12. Smith, H. L., and Horton, B. T.: Arteriovenous Fistula of Lung Associated with Polycythemia Vera: Report of a Case in Which the Diagnosis Was Made Clinically, Am. Heart J. **18**:589, 1939.

A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.
LOS ANGELES

FRANK HINMAN, M.D.
SAN FRANCISCO

ALEXANDER VON LICHTENBERG, M.D.
MEXICO, MEXICO

ALEXANDER B. HEPLER, M.D.
SEATTLE

ROBERT GUTIERREZ, M.D.
NEW YORK

LIEUTENANT COMMANDER GERSHOM J. THOMPSON (MC), U.S.N.R.

EDWARD N. COOK, M.D.
ROCHESTER, MINN.

EGON WILDBOLZ, M.D.
BERNE, SWITZERLAND
AND
VINCENT J. O'CONOR, M.D.
CHICAGO

KIDNEY

Anomaly.—Jacobs [1] describes an unusual type of horseshoe kidney, which presents different features from those of the usual form of this anomaly, and places it in the group of unsymmetric horseshoe kidneys. The patient, a woman aged 45, had suffered from recurrent attacks of abdominal pain characteristic of "horseshoe kidney disease" and had undergone appendectomy previously without benefit. The right ureter could be catheterized up to 20 cm., at which point the catheter stopped. A retrograde pyelogram of the right side showed an elongated boat-shaped pelvis lying over the body of the fifth lumbar vertebra, with calices projecting upward, downward and laterally from both extremities of the pelvis. The ureter left the lower margin almost at its midpoint and passed to the right sacroiliac joint, whence it descended almost vertically to the bladder. A subsequent retrograde pyelogram of the left kidney showed the typical characteristics of a horseshoe kidney, with its fusiform pelvis at the level of the third lumbar vertebra. A group of lower calices was directed medialward and another downward on the inner aspect of the ureter. It seemed obvious from these appearances that the two organs were fused.

At operation, which was carried out transperitoneally, a flat renal mass was revealed, with the hilus and the pelvis situated anteriorly, joined to the lower pole of the left kidney by a broad, thick isthmus of parenchymatous tissue. A shallow vertical furrow on the anterior surface of the isthmus indicated the site of union of the two organs, but the posterior surface was devoid of any such marking. Both ureters crossed the front of the isthmus. Of the various irregular vessels encountered in freeing and mobilizing the right kidney, an artery and a vein, which descended together from the main abdominal vessels to the upper end of the sulcus, were the most prominent. These bifurcated halfway down the sulcus, a branch passing to each segment. They were secured just above the point of bifurcation. The isthmus was cut through in a wedge-shaped manner, and the right kidney was removed. Drainage was provided extraperitoneally by way of a stab incision in the right iliac fossa, and the peritoneal cavity and the abdominal wall were sutured without drainage. The patient made an excellent recovery, and there has been no recurrence of the attacks of pain. A subsequent retrograde pyelogram of the left side showed that the lower pole had moved outward and that in consequence the ureter left the kidney on the medial side of the downward projected calix instead of on its lateral side. In addition, the ureter had lost its "flower vase" curves.

Examination of the specimen leaves little doubt that it is the lower pole of the right seg-

The opinions and the assertions contained herein are the private ones of the various writers and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

1. Jacobs, A.: Rare Variety of Horseshoe Kidney, Brit. J. Urol. **15**:55-59 (June) 1943.

ment that is united to the lower pole of the left and that the anomalous condition is therefore an unsymmetric horseshoe kidney and not a connecting link between the horseshoe kidney and the "long" kidney, in which the fused organs lie to one side of the median line and are the result of fusion of dissimilar poles.

Abeshouse [2] states that congenital anomalies of the kidney are susceptible to the same pathologic complications as is the normally developed kidney. Complete urologic examination is of inestimable value in diagnosis and treatment of renal anomalies. The possibility of a renal anomaly must be borne in mind by the urologist and the surgeon in cases in which there is an obscure abdominal, pelvic or retroperitoneal mass and in those in which there are ill defined symptoms of renal origin.

The treatment of pathologic complications in cases of anomalous kidney depends not only on the type of anomaly but on the character of the symptoms and the extent of renal damage and functional impairment. Patients who do not have symptoms and who do not present any renal pathologic condition do not require any treatment. Such patients should be informed of the anomaly and advised to return for reexamination at frequent intervals.

The successful surgical treatment of an anomalous kidney demands an orderly plan of operation: proper surgical approach, that is, an operation carried out extraperitoneally through a lumbar or a lateral abdominal incision; careful attention to the vascular supply; accurate hemostasis of parenchymal incisions; proper disposition of the ureter; adequate drainage of the kidney and the renal fossa, and accurate closure of the operative wound. The operative results which were obtained in 56 cases of renal anomaly reported by Abeshouse were uniformly good; there were no deaths.

Zide and Maher [3] report 2 cases of crossed renal ectopia, a condition in which one kidney is displaced to the side opposite its normal position and lies below the kidney of that side, to which it may or may not be fused. Its ureter crosses the midline and then passes down to enter the bladder normally. When fusion occurs, the resulting renal mass presents a peculiar, bizarre outline, variously described as a sigmoid or a tandem kidney. The blood supply for these kidneys is usually posterior and arises from the nearest arterial source. The branching and the course of the arteries do not follow any set pattern. Usually the venous return accompanies the arterial supply. Fixation of the ectopic kidney is due to surrounding adhesions, as well as to aberrant blood vessels. The ptosed kidney, on the contrary, is supplied by vessels which have a higher derivation and a downward course to the kidney. The pelvis, which is usually extrarenal, is located on the ventral, or anterior, aspect of the organ. The patient's symptoms depend on the function and the location of the ectopic kidney and the complications which have occurred.

One of the patients was a man, aged 28 years, who had urgency and frequency of urination. The urine contained a moderate amount of pus. Cystoscopy with roentgenograms taken after the catheters had been passed showed that the right ureteral catheter followed a normal course to the region of the right kidney, while the left ureteral catheter passed from the left side of the pelvis, across the sacrum to the right side of the midportion of the fourth lumbar vertebra. Pyelography showed a normal right renal pelvis and calices, while the left kidney failed to fill except for the calices in the upper part of the pelvis, which contained a small amount of opaque medium.

The second patient with crossed renal ectopia was a youth aged 19 who had abdominal pain which was aggravated by strenuous activities and alleviated by rest. The urine was normal. Intravenous urograms revealed that the left kidney was normal in size, location and function but that the right kidney was located in the left side of the pelvis superimposed on the fifth lumbar vertebra and the first sacral segment. Cystoscopy revealed normal mucosa of the bladder and normal ureteral orifices. Retrograde pyelograms showed a normal left kidney and ureter. The right ureteral catheter coursed from the right side of the bladder across to the left side of the bony pelvis, where the calices and the renal pelvis of the right kidney were poorly filled but appeared normal grossly.

Tumor.—Moore [4] presents a case of mixed tumor of the kidney in an adult. A review of the literature reveals that 26 cases of this disease among adults have been reported. The growth is malignant, and cures are unusual. The patient, a man aged 56, was admitted to the hospital in 1939. In 1914 he had had an injury of his right loin. Two years later he had had several attacks of hematuria and renal colic on the right side. For the last ten years before admission to the hospital he had a swelling in the right side of

2. Abeshouse, B. S.: Surgery of the Congenital Anomalous Kidney, Surg., Gynec. & Obst. **78**:288-303 (March) 1944.

3. Zide, H. A., and Maher, E. J.: Crossed Renal Ectopia: Report of Two Additional Cases, J. Urol. **50**:560-563 (Nov.) 1943.

4. Moore, T.: A Mixed Tumor of the Kidney in an Adult, Brit. J. Surg. **30**:381-384 (April) 1943.

the abdomen, which became much larger before his death. In 1923 an examination had revealed a tumor of the right kidney which was partially calcified. A diagnosis of hypernephroma was made. Examination (in 1939) showed a large tumor filling the right side of the abdomen. No surgical treatment was carried out; the patient rapidly became sicker and died. At necropsy a large renal tumor was found occupying the entire right side of the abdomen. Histologic examination showed that it was a mixed tumor. The main point of interest in this case is the length of time the tumor was definitely known to have been present—sixteen years.

Weisel, Dockerty and Priestley [5] review from clinical and surgical aspects and end results the records of 35 cases of renal sarcoma. The authors conclude:

> Renal sarcoma is a rare tumor characterized by rapid growth and early and widespread metastasis. Clinical distinction from other types of renal malignant lesions is rarely possible. The treatment of choice is early radical removal of the affected kidney along with the "unruptured" tumor and a generous amount of perirenal fat. Roentgen therapy may be administered after operation in an effort to improve the end results which, on average, will yield but 10 per cent of 5 year survivals. Pathologically, sarcomas arise from the connective tissue of the renal cortex and medulla, from the capsular peripelvic smooth muscle tissue and from the peculiar fibrolipomatous elements found in the renal capsule. The tumors can be classified satisfactorily according to these three tissues of origin.

Weisel, Dockerty and Priestley [6] report a clinicopathologic study of 44 cases of Wilms's tumor of the kidney. The records of 101 patients who were seen at the Mayo Clinic from 1904 to 1940 inclusive and whose condition was diagnosed as Wilms's tumor, embryonal sarcoma, mixed tumor of the kidney or sarcoma of the kidney were reviewed carefully from the standpoints of clinical data, treatment and end results. Pathologic material was available from 85 cases and was studied in gross detail, with special reference to color, size and degree of encapsulation as well as to the relation of the tumor to the residual renal substance.

Wilms's tumor occurs once among approximately 25,000 patients coming to the clinic. Twenty-nine of the 44 patients were female, and only 15 were male. The ages of the patients ranged from 7 months to 59 years; the largest number of patients were in the third year of life. The lesion affected the right kidney in 23 instances and the left in 21. Bilateral tumors, commonly reported in the literature, were not observed in the present series.

"Lump in the abdomen" and "swelling of the abdomen" were the chief complaints listed in the records of 34 patients. Hematuria was the cardinal symptom in 5 cases and apparently was considered of secondary importance in an additional 9. Pain was the presenting symptom in 3 cases but was present as a minor symptom in 5 other cases. Fever was noted in approximately half of the cases, and loss of weight and cachexia were observed in about a third. Symptoms were, in general, progressive, with an average duration of only four and a half months. In 39 cases physical examination revealed a mass or masses, variously described as being solid or cystic, firm, regular or irregular, not tender and generally unaffected by respiratory movements. In 20 instances the mass practically filled the abdomen. The presence of an abdominal mass was the most important single diagnostic sign of Wilms's tumor, although localization of the origin could not often be made on palpation alone. Ascites was noted in several cases, and in 2 there were signs of venous obstruction to the lower extremities. Evidence of emaciation was present in 15 cases, and in 15 the temperature varied from 99 to 104 F. Definitely elevated blood pressures were recorded in 4 cases.

Wilms's tumor was treated surgically in all of the 44 cases. Nephrectomy was performed in 42 cases, and exploratory operation with biopsy was carried out in 2. In 20 cases a transperitoneal approach was utilized and in 24 the posterolumbar route. In 34 cases the patients were treated by roentgen rays postoperatively, and in 21 of the more recent cases the patients received the benefit of such treatment as a preoperative measure. In this group of 21 cases good clinical results were observed in nearly all instances, as evidenced by marked reduction of the size of the neoplasm. Sometimes, indeed, it was this very shrinking process which decided whether or not operation should be done. Usually operation was performed when it was felt that maximal response to irradiation had been effected. This waiting period varied from two to six weeks, with a tendency toward earlier operation among the more recent cases in the series.

At the time of this study 37 of the 44 patients were dead. Of these, 1 died in the hospital after operation. Thirty of the remaining 36 died from the effects of the tumor within twelve months. The 2 patients who had been subjected to exploratory operation and biopsy succumbed two

5. Weisel, W.; Dockerty, M. B., and Priestley, J. T.: Sarcoma of the Kidney, J. Urol. **50**:564-573 (Nov.) 1943.

6. Weisel, W.; Dockerty, M. B., and Priestley, J. T.: Wilms' Tumor of the Kidney: A Clinicopathologic Study of Forty-Four Proved Cases, J. Urol. **50**:399-413 (Oct.) 1943.

and nine months respectively after operation. Five patients survived for one to two years, and 1 patient died four years after operation.

The tumors were all unilateral. The size varied from 30 by 15 by 12 cm. to 4 by 3 by 2.5 cm.; all but 2 of the specimens were larger than the normal kidney. Nearly all of the specimens demonstrated degrees of encapsulation; 33 were more or less nodular or lobulated, the remainder being globoid or unicentric.

Weisel, Dockerty and Priestley state that from a review of the literature and an analysis of their material it appears that Wilms's tumor of the kidney, although rare, is one of the most common tumors of childhood and that it is a tumor of infancy and adolescence, because 37 of their 44 patients were less than 12 years of age.

The tumors were insidious in their onset and relentless in their course. A large abdominal mass of relatively short duration was a symptom in no less than 39 of their 44 cases.

The pathologic change induced by roentgen therapy was among the most interesting features in the study. Widespread necrosis of tumor cells was almost always evident in cases in which roentgen therapy was used. The necrosis reflected the clinical observation of reduction of the size of the neoplasm. It was observed, however, that viable nests of highly malignant cells persisted in these regions of radionecrosis. From the pathologic standpoint, therefore, it would seem unwise to allow a protracted period to elapse between the date of the last roentgen treatment and the time of operation.

In the earlier days nephrectomy alone was employed most frequently. Later, nephrectomy followed by postoperative roentgen therapy was used rather widely. During recent years the immediate effectiveness of roentgen rays in diminishing the size of these tumors has become widely appreciated, and as a result this form of treatment has been employed prior to operation as well as after nephrectomy. Some have gone so far as to employ roentgen therapy alone in the treatment of Wilms's tumor. In general, treatment has been discouraging, and any possibility of improving the ultimate results in the management of this condition would be most welcome.

At present five main forms of treatment are employed: (1) roentgen irradiation alone, (2) operation alone, (3) roentgen irradiation followed by operation, (4) operation followed by roentgen irradiation and (5) irradiation followed by operation and subsequent further irradiation. All writers agree that treatment with roentgen rays exerts a remarkable effect on the size of a Wilms tumor within a few weeks after its administration; however, Weisel, Dockerty and Priestley do not know of any case in which a five year cure of this disease has been established in this manner. In other words, there seems to be little evidence to support the treatment of Wilms's tumor by irradiation alone. Except in 1 case viable tumor tissue was found when nephrectomy was performed after a preliminary course of irradiation.

There appears to be little support for treatment of Wilms's tumor by nephrectomy alone. Inasmuch as treatment with roentgen rays exerts such a pronounced effect on lesions of this type, there seems to be no good reason why it should not be utilized at some time in the management of these growths. If it is not employed preoperatively, it may be used postoperatively. The preferable form of treatment of Wilms's tumor is immediate nephrectomy, if the tumor is small enough to be removed without undue hazard or risk, followed by postoperative irradiation. If the tumor is larger, a brief course of preliminary irradiation extending over two to three weeks followed by nephrectomy and subsequent further irradiation seems desirable.

Resection.—Mathé [7] states that resection of the kidney is of inestimable life-saving value and should be used more extensively than at present. It is conceded that half of one kidney will sustain life. Indications for partial renal resection apply to localized benign pathologic processes in which it is anatomically possible to resect a portion of the kidney without destroying the blood supply to the remainder of the organ. Contraindications are tuberculosis, malignant lesions and war injuries which are not available for immediate treatment. Meticulous technic, including preliminary ligation of nutrient blood vessels, approximation of flaps of parenchyma with atraumatic needles and nephropexy assure success. The mortality rate is about 5 per cent, and the morbidity rate is insignificant. Function is reduced in approximate proportion to the amount of secreting renal tissue resected. Data on 13 cases of which Mathé had first hand knowledge are reported.

McKim, Smith and Rush [8] were unable to find any recorded instance in which both nephrectomy and heminephrectomy had been performed on a human being successfully. They report a case in which a woman has lived twelve years with half of one kidney. During this period

7. Mathé, C. P.: Partial Resection of the Kidney: Report of Thirteen Cases, J. Urol. **50**:525-542 (Nov.) 1943.

8. McKim, G. F.; Smith, P. G., and Rush, T. W.: Twelve Year Survival with One-Half of One Kidney, J. Urol. **50**:769-774 (Dec.) 1943.

she has led a normal life and with the exception of a pregnancy, a cholecystectomy and recently the menopausal cycle has been perfectly well.

The patient, a woman aged 38 years, was first treated in 1930, at which time retrograde pyelographic studies showed extensive calculous pyonephrosis on the left side, with a stone impacted in the upper end of the left ureter; on the right there were massive calculous pyonephrosis of the upper half of the double kidney and a moderate degree of extrarenal hydronephrosis of the lower half, which was not infected and was free of stones. Nephrolithotomy on the left kidney was done, and a nephrostomy tube was left in place. The patient made an uneventful recovery. Four weeks after drainage of the left kidney, heminephrectomy on the right kidney was done. Seven months later pyelotomy on the right kidney was performed, and two months after this nephrectomy of the left kidney was done. Ten months later the stone, which was acting as a foreign body and preventing the healing of the sinus, was removed from the left ureter. Four years after the original admission to the hospital it was found that the patient's right kidney was functioning normally. Tests of renal function in 1943 showed a concentration of urea of 28 mg. per hundred cubic centimeters of blood, and with the exception of hypertension the patient was in good general condition.

Cysts.—Braasch and Hendrick [9] state that renal cysts become of clinical significance only when they become so large or so numerous as to cause renal dysfunction or when they become apparent on physical or urographic examination.

Large simple cysts frequently are observed on clinical examination. Their existence usually can be inferred by means of urography, although exact diagnosis may be uncertain. Urography, either excretory or retrograde, offers the simplest form of diagnosis. The excretory urogram will offer sufficient diagnostic data in many cases but not in all. Greater accuracy usually is obtained by the retrograde urogram. Absence of deformity in the pelvic outline and unsatisfactory urograms are common causes of diagnostic failure.

The differentiation of urographic deformity caused by renal cyst from that caused by renal neoplasm may be exceedingly difficult, and failure to distinguish between the two deformities is a frequent cause of diagnostic error. In most cases surgical exploration will be advisable in order to establish an accurate diagnosis.

Multiple simple cysts may be confused easily on surgical exploration with polycystic disease. Multilocular cysts differ from the ordinary type of multiple simple cyst in that a single large cyst is subdivided into smaller segments. Peripelvic (pyelogenic) cysts differ from simple renal cysts in causation, clinical course and treatment. Cystic hypernephroma occasionally is observed and may be confused with simple cyst, both on clinical examination and on casual surgical examination.

The infrequent occurrence of hypertension caused by simple cysts is in contrast to the frequent incidence of hypertension in cases of polycystic disease.

Aspiration of cysts as a diagnostic procedure occasionally may be indicated in cases in which surgical exploration is not advisable. The procedure, however, may be unsatisfactory because of possible error of diagnosis and complications which may follow it. Surgical exploration usually is more satisfactory, and surgical excision of the cyst is a better treatment.

McCrea [10] states that the most frequent site of origin of a solitary renal cyst is the lower pole of the kidney. Next in frequency is the upper pole and lastly the body of the kidney. The condition may be observed at any time but is not commonly seen in the first two decades of life. It occurs most often between the ages of 30 and 50 years. The most logical treatment is resection of the cyst. However, nephrectomy may be advisable because of extensive destruction of the kidney or because of uncontrollable hemorrhage after resection of the cyst.

Perinephric Abscess.—Swan [11] presents data on 26 proved and 6 possible cases of perinephric abscess in infants and children. To classify lesions on an etiologic basis as metastatic, complicated by underlying renal disease or secondary to trauma to the kidney is important for prognostic and therapeutic reasons. If the patient is a child, a history which includes urinary symptoms or a finding of albumin or white blood cells in the urine strongly suggests a complicated type of lesion and indicates a thorough study of the urinary tract. Intravenous pyelography should be done preoperatively on all patients suspected of having perinephric abscess, unless they are too ill to tolerate the procedure.

Treatment varies with the type of abscess. With the metastatic variety, as soon as the diagnosis is reasonably established incision and drain-

9. Braasch, W. F., and Hendrick, J. A.: Renal Cysts, Simple and Otherwise, J. Urol. **51**:1-10 (Jan.) 1944.

10. McCrea, L. E.: Solitary Cyst of the Kidney: Report of Two Cases, Am. J. Surg. **60**:328-334 (June) 1943.

11. Swan, H.: Perinephric Abscess in Infants and Children: A Study of Twenty-Six Patients Surgically Treated, Am. J. Surg. **61**:3-10 (July) 1943.

age are performed. Occasionally a patient is seen who has a history and physical findings suggesting infection in the perinephrium but whose constitutional reaction is not severe. Swan had 6 patients whose history and physical findings when first seen suggested perinephric abscess but who recovered completely with conservative therapy and observation, without surgical treatment. It is Swan's belief, though of course in these cases the diagnosis was not established, that these patients probably had cortical abscesses and perhaps some inflammation of the perinephrium but that the defenses of the body overcame the infection and no softening or formation of abscess occurred.

In Swan's group of 11 cases of metastatic perinephric abscess, the average duration of the history of symptoms was two weeks; the average preoperative delay in the hospital was four days. There were no deaths in this group.

The treatment and prognosis of the complicated variety are different and must be individualized. Therapy is twofold: immediate treatment of the perinephric abscess and subsequent treatment of the underlying lesion of the urinary tract. Intravenous pyelography usually can be done preoperatively.

The term of hospitalization and the mortality rate for complicated perinephric abscess have been forbidding. The total stay in the hospital of the patients with complicated perinephric abscess averaged seventy days. The mortality rate was 45 per cent, 5 of the 11 patients succumbing sooner or later to their underlying lesion.

The prognosis and treatment of post-traumatic abscess are similar to those of metastatic abscess. Early drainage is usually all that is needed. There were no deaths in Swan's group of cases.

Pyelonephritis.—Prewitt [12] states that in a series of 667 cases in which necropsy was performed there were 58 cases of pyelonephritis (all types: obstructive, nonobstructive, acute and chronic), an incidence of 8.69 per cent. The age incidence was from 19 to 87 years.

The associated pathologic conditions have been tabulated to show that in pyelonephritis obstruction to urinary outflow is fairly common and, when present, usually overshadows the pyelonephritic process.

The presence of pus cells in the urine is significant. In 11 (32 per cent) of 37 cases of chronic pyelonephritis there were occasional pus cells in the urine, and in 23 (62 per cent) there were from 1 to 4 plus pus cells in the urine. In 28 of 32 cases in which a urinary culture was made there was a positive culture. Bacillus coli was the predominating organism.

Tuberculosis.—Corbitt [13] states that renal tuberculosis often is associated with secondary bacteriuria. He has reviewed the clinical records of cases of tuberculosis of the kidney found at the Mayo Clinic in the past ten years. These cases, which numbered approximately 775, meet the following qualifications: 1. Catheterized ureteral specimens had been collected from the kidney or kidneys involved. 2. These specimens had been stained with Gram's stain, cultured or both. 3. Positive evidence of renal tuberculosis had been recorded on the basis of one or more of the following data: presence of bacilli, indicated with acid-fast stain, positive results for tuberculosis on inoculation of guinea pigs or signs of renal tuberculosis revealed by pathologic examination after nephrectomy.

There were 213 specimens which met these qualifications. In 62 (29.1 per cent) of these 213 specimens secondary bacteriuria was found. Of these, 53 showed positive Gram staining and 30 gave positive cultures. Of the 30 that had a positive culture, 9 had negative Gram staining. The organism found most commonly was Escherichia coli, which was present in 40 per cent of the positive cultures. Pseudomonas was found in 23 per cent of the specimens.

Nephrosis.—Schwarz, Kohn and Weiner [14] review their observations of cases of lipid nephrosis made during a period of twenty years. During this time they made a diagnosis of the condition for 40 children, 22 of whom died. Eight patients were followed from seven to twenty years. Four of these children had hypertension and increased urinary sediment counts at the time of the report. Two others had increased urinary sediment counts only. The beneficial effect of an acute infection during the edematous phase is discussed. The histologic observations in 12 necropsies are reviewed. One cannot predict the pathologic changes in the kidneys from the clinical course. Schwarz and his associates conclude, therefore, that most children who have the classic clinical picture of lipid nephrosis have a glomerular involvement but perhaps in a different form from that observed in chronic or subacute glomerular nephritis.

12. Prewitt, G.: Pyelonephritis, West. J. Surg. **51**: 450-457 (Nov.) 1943.

13. Corbitt, R. W.: Secondary Bacteriuria Associated with Renal Tuberculosis, J. Urol. **51**:11-13 (Jan.) 1944.

14. Schwarz, H.; Kohn, J. L., and Weiner, S. B.: Lipid Nephrosis: Observations over a Period of Twenty Years, Am. J. Dis. Child. **65**:355-363 (March) 1943.

Hypertension.—Bugbee [15] reports a case of hypertension of renal origin as observed at operation on a single kidney. The patient was a man, 52 years of age, whose left kidney had been removed for what was said to be a renal papilloma. On examination, there was tenderness in the right side of the abdomen, but the kidney could not be palpated. The urine contained a trace of albumin and sugar and numerous pus cells. Excretory urograms showed good function of the kidney, the dye outlining the ureter to the level of the ureterovesical junction, at which point there was an impacted calculus. With increased administration of fluids and conservative treatment, the urinary output was increased. An attempt was made to pass a catheter to the right kidney, but an obstruction was felt just above the bladder. No urine was seen coming from the right ureteral orifice. The right kidney was exposed surgically and was found to be enlarged and congested. When traction was made on the renal pedicle, the blood pressure, which had been 120 systolic and 58 diastolic, rose considerably. Pressure on the renal artery caused the reading to go to 160 systolic and 100 diastolic and 230 systolic and 120 diastolic. With relief of pressure and traction on the pedicle, the pressure subsided to 120 systolic and 80 diastolic. Repeated traction and pressure on the pedicle caused the same condition to recur several times. The kidney was drained, and later the stone was removed. The postoperative course was normal, and the patient did not have any urinary symptoms after the operation.

Braasch and Strom [16] reviewed 50 cases in which there was clinical evidence of renal trauma and found that although renal injury may be related to hypertension it is not a common cause. Nephrectomy was performed in 5 of these cases. Hypertension existed in 3 of these 5 cases, but after removal of the kidney the blood pressure returned to normal. In the other 2 cases, the preoperative blood pressure was normal. The small number of patients having renal injury who underwent nephrectomy would corroborate the value of conservative treatment.

In 38 of 45 cases in which no operation was indicated, the blood pressure was normal subsequent to renal injury. In 6 of the other cases, the degree of hypertension was moderate and the hypertension either existed prior to renal injury or was explained by factors other than renal. In only 1 of these cases was renal trauma considered a possible factor in the production of hypertension.

Apparently the changes in the renal tissue after injury usually do not cause hypertension. In those cases in which operation was not indicated, it is evident either that the injured renal tissues healed or that moderate, mild circumscribed cicatricial changes resulted.

Hypertension due to renal trauma usually occurs in cases in which there is secondary renal infection. This is in keeping with the fact that changes of the renal tissues secondary to chronic infection have been noted in most renal lesions which are known to cause hypertension.

Renal Lesions.—Deming,[17] in order to determine the type and the incidence of renal lesions in men within the draft age, made a study of 330 men between the ages of 18 and 38 years who had renal lesions.

Renal and ureteral calculi comprise almost 50 per cent of the lesions. Ureteral calculi were included, because it was evident from the history and from the cystoscopic and roentgenographic findings in these cases that the ureteral calculi began their existence in the kidney. There were 154 men in this age group who had renal and ureteral calculi. Fourteen patients (9 per cent) gave histories which indicated a familial factor. Eight patients gave histories which suggested that they had had renal calculi in the predraft age. Fifty-nine had had symptoms for six months or less; the remainder, all the way up to twenty years. The older the patients, the more frequent was the occurrence of calculi. There were 6 patients in the latter part of the second decade of life, 65 patients in the third decade of life and 83 in from the thirtieth to the thirty-eighth year. Infections existed on admission to the hospital or appeared at some time during the passage or the removal of the calculi in 33 cases (34.5 per cent). Bilateral ureteral calculi were found on admission of the patients to the hospital in only 5 instances. Recurrent calculi in the same kidney occurred in 13 cases and in the opposite kidney in 6 cases. One patient was free of calculus formation for sixteen years before recurrence. Forty-four patients who had renal or ureteral calculi (29 per cent) had associated pathologic changes within or outside of the genitourinary tract.

Treatment consisted of nephrectomy, immediate or eventual, in 11 cases, surgical removal of the calculus in 37 and cystoscopic removal in 78 (50 per cent). The stone passed spontaneously in 11 cases.

15. Bugbee, H. G.: Hypertension of Renal Origin as Observed at Operation on a Single Kidney, J. Urol. **50**:647-651 (Dec.) 1943.

16. Braasch, W. F., and Strom, G. W.: Renal Trauma and Its Relation to Hypertension, J. Urol. **50**:543-549 (Nov.) 1943.

17. Deming, C. L.: Renal Lesions Within the Draft Age, J. Urol. **50**:641-646 (Dec.) 1943.

The group of cases of pyogenic renal infection comprises 38 cases of pyelitis and 5 of pyelonephritis. In 11 cases of pyelitis the infecting organism was Staphylococcus aureus; in 22, Bacillus coli; in 1, Bacillus alkaligenes, and in 1, Bacillus mucosus capsulatus. In 14 cases the infection was bilateral. Twenty-four patients were cured entirely of their infection, 8 were improved, 2 were unimproved and 4 were seen only once or twice. A few of these patients were treated with sulfonamide compounds.

There were only 5 patients with pyelonephritis. Two had bilateral infections with moderate elevation of systolic blood pressure. Two were treated by nephrectomy, 1 of whom recovered and the other of whom died in three years. The other 3 improved, but the infections never subsided completely.

Hydronephrosis in early adulthood is a comparatively common condition of men. It occurred in 29 cases (8.8 per cent) in this series. Eight patients had bilateral lesions. Sixteen patients had symptoms of less than one year's duration, while 1 had had periodic symptoms for twenty-six years. Only 2 had slight elevation of blood pressure. Eight were treated by nephrectomy and 12 by various plastic procedures on the ureteropelvic junction and nephropexy. Four were treated by dilation of the ureter.

Trauma of the kidney occurred as frequently as hydronephrosis. Twenty-three of the 29 patients were in their early twenties. Most of them were injured in automobile accidents or while playing football. Twenty-four recovered with expectant treatment. Five had nephrectomy. In 5 cases infections of the injured kidney developed. In 1 case the infecting organism was B. coli and in 4 it was Staph. aureus. There were no deaths. In most cases cystoscopy was performed when the kidney was healed. The pelvis apparently healed completely. However, the function of two of the healed kidneys was diminished, as indicated by the functional phenosulfonphthalein test. All infections were controlled.

Tuberculosis of the kidney occurred in 21 cases. In 3 instances one parent had died of tuberculosis. Bilateral renal disease was present in 5 cases. Fourteen, or two thirds, of the patients were less than 25 years of age. Only 3 had symptoms dating back to the eighteenth year or earlier. Thirteen patients were treated by nephrectomy and partial ureterectomy, 10 on the right side and 3 on the left. The results show that 12 patients are apparently well. Three are living but have tuberculosis; 5 have moved away and their present condition is not known, and there has been 1 death.

Hematuria of unexplained origin occurred in 12 cases. Thorough investigative measures were employed and repeated without determining the etiologic factor. None of the patients passed stones or had an infection of any kind in the urinary tract. The duration of their hematuria ranged from three days to two years.

Anomalies of the kidneys were infrequent—more infrequent than those of the kidneys of the average group of patients examined.

Ptosis of the kidney is rare among men. Five of the 6 patients who had nephroptosis were past 30 years of age. The symptoms of pain in the kidney lasted from three weeks to ten years. Only 1 patient had surgical nephropexy.

A diagnosis of phosphaturia was made in 4 cases. In these cases the duration of symptoms of urinary irritation and frequency with a small vesical capacity extended from five days to twelve years, with visits to many physicians without relief. None of the patients had infections of the urinary tract or calculi demonstrable by cystoscopic and roentgenologic examinations. In 3 cases the condition was controlled by ingestion of dilute hydrochloric acid, while in the fourth there was not much improvement after two months of treatment.

Nephrosis as such occurred in 3 cases. In 1 case there was a familial history of cardiorenal disease. In the other 2 there were histories of prolonged symptoms of seven years or more. Albuminuria, low specific gravity of the urine, diminished renal function and elevated blood pressure were present. The patients were all treated in a conservative manner, without any appreciable improvement.

Renal tumor occurred in only 1 case.

The peak of adult renal health undoubtedly occurs before the fortieth year. Thirty-one, or almost 10 per cent, of the patients had either a familial factor of renal disease or symptoms of renal disease before the age of 18 years.

URETER

Anomaly.—Wilson and Herzlich [18] report a case of postcaval ureter. Medical literature contains reports of only 27 cases. These include cases found at necropsy as well as at operation. Of all cases recorded, in only 1 has the condition been diagnosed preoperatively. Cases of right postcaval ureter as well as of bilateral postcaval ureter have been observed. In the latter condition there is a double vena cava with each ureter passing behind its respective vein. The present opinion unanimously ascribes the fault to the embryonal vascular system rather than to the

18. Wilson, C. L., and Herzlich, J.: Post Caval Ureter, J. Urol. **51**:14-18 (Jan.) 1944.

urinary system; for this reason the anomaly has not been classed with ureteral abnormalities. From the clinical standpoint, however, it may well be placed in the latter group.

Wilson and Herzlich's patient complained of typical renal colic on the right side. The symptoms had begun about six months prior to admission to the hospital, at which time the patient noted intermittent attacks of pain in his right loin. Retrograde pyelograms revealed an essentially normal left kidney and ureter. The right kidney was found to be severely hydronephrotic. At operation the renal pelvis was identified and was traced downward. The upper portion of the ureter was dilated to 3/4 inch (2 cm.) in its widest diameter. This was traced down for a distance of approximately 3 inches (8 cm.), at which point it was noted that the ureter passed medially and crossed beneath the inferior vena cava. It could be demonstrated definitely that the ureter passed completely beneath the vein and that the portion beneath the vein was of normal size but was compressed. The ureter below this level was normal in size and appearance. The ureter was ligated and divided approximately 1 cm. lateral to the vena cava. The renal pedicle was exposed and was found to be extremely short. The pedicle was doubly clamped, ligated and divided, and the kidney was removed.

Transplantation.—Stevens and Marshall [19] discuss reimplantation of the ureter into the bladder. The need for the operation is apparently most frequent after vesical resection for neoplasms involving a ureteral orifice, but reimplantation will be employed in the occasional case of accidental injury to a ureter, of obstruction of the lower part of the ureter due to intrinsic or neighboring disease or to diverticulum of the ureter or the bladder. The methods employed for reimplantation of the ureter into the bladder may be divided into two groups—with the ureter (1) running directly into the lumen of the bladder through a stab wound or (2) entering obliquely according to nature's usual rule governing the entrance of conducting tubes into cavities. Sutures are sometimes placed outside the bladder, through the ureteral and vesical walls; sometimes they are used only within the bladder, or they may be placed both inside and outside the bladder. Within the bladder, the end of the ureter may be slit on one side only, to make a long elliptic opening, and the end fastened to the vesical mucosa and submucosa only or by penetrating sutures to the whole thickness of the vesical wall. Or the distal centimeter of the ureter may be split in two and each flap secured to the bladder.

Realizing that obstruction is a large factor in vitiating results and that infection also plays a major role, Stevens and Marshall have been trying a simple technic during the past three and a half years. The operation is always carried out extraperitoneally. To diminish formation of fibrous tissue drains are so placed that only rubber tissue is in contact with the tissues and the drains are removed early. Tension is avoided. Sutures are used only inside the bladder and penetrate mucosa and submucosa only, and the bladder is kept at rest by suprapubic drainage. Fine chromic sutures—no. 0000—are used. No deleterious results have been noticed from having the knots within the bladder. Sulfadiazine is used to control infection. In 2 cases, one suture was used outside the bladder, placed in the periureteral tissue, but otherwise none was employed.

A small incision is made at the appropriate place on the vesical wall, penetrating muscle only. A rather pointed curved clamp bluntly dissects a channel under the mucosa downward toward the vesical outlet for about 2 cm. A small incision is made through the mucosa over the end of the clamp. Working through a suprapubic vesical opening, another clamp is passed retrograde through this channel and grasps the ureter, the distal centimeter of which has been bisected, to form a "fish-mouth." The ureter is drawn into the bladder through this channel, and the two ends are each fastened to the vesical mucosa and the submucosal tissues.

Reports of data on 10 patients are given. Nine of the patients had carcinoma of the bladder, and 1 had low fibrous ureteral obstruction. Urograms made before and after operation demonstrate little or no dilatation of the upper part of the urinary tract after operation in 5 cases in which the urograms had been normal before operation. Ureters dilated before operation have remained so afterward. Increased ureteral dilatation, as noted in the late postoperative pyelogram, was seen but once. In that instance the patient probably had local recurrence of carcinoma. There were no perivesical abscesses or fistulas.

In all cases function of the kidney on the side on which the operation was performed, as demonstrated in the five minute films of the excretory urogram series, was as good after operation as before, or better.

In 2 of 4 cases in which cystograms were taken postoperatively there was no ureteral reflux

19. Stevens, A. R., and Marshall, V. F.: Reimplantation of the Ureter into the Bladder: Report of a Method Applied to Ten Patients, Surg., Gynec. & Obst. 77:585-594 (Dec.) 1943.

some months after operation; there was slight reflux eight months after operation in 1 case in which the ureter had been dilated and thickened above a fibrous obstruction, and there was definite reflux a few weeks after operation in the fourth case.

Higgins [20] reviews 19 cases of transplantation of the ureters into the rectosigmoid of infants.

Exstrophy of the bladder is classified into four types as follows: (1) fissura vesicae superior, in which there is a normal union of the pubis but a defect in the upper part of the bladder; (2) fissura vesicae inferior, in which the symphysis is developed normally but the bladder is split inferiorly; (3) typical complete exstrophy, in which the symphysis pubis is absent with varying degrees of separation of the pubic bones; (4) exstrophy of the bladder complicated by intestinal openings on the extroverted area.

In the third type the everted bladder protrudes above the level of the surrounding abdominal wall. In male patients, epispadias is always present. The prostate may be absent, or cryptorchism may occur. At times a bifid scrotum may be observed. In the female patients the clitoris is cleft, the labia are rudimentary and the urethra forms an open sulcus. A double vagina or a bicornate uterus may also be present.

The age for transplanting the ureters into the rectosigmoid for the relief of children suffering from exstrophy of the bladder merits serious consideration. Without surgical intervention 50 per cent of the children die before the age of 10 years and 66 per cent succumb before the age of 20 years. In the majority of instances renal sepsis and renal failure are directly responsible for early death. It is usually advocated that operation be postponed until the child is 4 to 6 years of age and until he has gained control of the rectal sphincter.

This recommendation ignores the fact that children less than 5 or 6 years of age experience repeated attacks of pyelitis or pyelonephritis and that in many instances death occurs before the child has attained 4 or 5 years of age. Obstruction frequently develops at the ureterocystic junction on the exposed bladder, producing hydroureter and hydronephrosis, which not only may be conducive to infection of the upper part of the urinary tract and destruction of renal parenchyma but may render transplantation of the ureters into the bowel technically impossible or in some instances may necessitate removal of one kidney. Thus ureterocystic obstruction may produce stasis, followed by infection, renal sepsis and impairment of renal function, resulting in death of the child during the first two or three years of life unless surgical intervention is undertaken.

In view of results secured during the last three or four years, Higgins believes that the operation should be performed on infants during the first year of life, preferably during the first six months, for the following reasons: 1. Just as the infant tolerates the trauma of passing through the birth canal, it tolerates surgical procedures extremely well. As is attested by the results in other fields of surgery, delay is not countenanced; plastic operations for harelip, the Rammstedt operation for pyloric obstruction, operative intervention for intussusception or strangulated hernia and other surgical procedures are performed without hesitation. 2. Recurrent attacks of renal infection may result in sepsis and death before the child is 4 to 6 years of age. 3. The organisms in the bowel of infants less than 6 months of age probably are less virulent than those in older children and in adults. 4. Because of ureterocystic obstruction, the ureter may dilate sufficiently to render its transplantation into the bowel technically impossible. Although one ureter may be transplanted, hydronephrosis on the opposite side may require removal of the kidney. 5. If the operation is performed early in life, the child may develop normally both physically and mentally. 6. The operative mortality rate and the morbidity rate are low. 7. The tone of the rectal sphincter, in Higgins' experience, has always been adequate to prevent leakage of urine from the rectum after the sphincter starts to function normally. 8. Because of the parents' attachment to the child, it is better that if death should result from operation it should occur before ties are established.

The purposes of the preoperative routine are to cleanse the bowel completely of fecal contents and to sterilize the bowel as far as possible.

The operation is performed while the child is under ether anesthesia. Higgins does not recommend the simultaneous transplantation of the ureters into the rectosigmoid of infants less than 1 year of age. Transplantation of the right ureter should be done first, followed in ten days by transplantation of the left ureter into the bowel. The exstrophic bladder may be removed at this time. The plastic operation to correct the epispadias should be delayed until the child is 5 or 6 years of age. Technically, transplantation of the ureter into the bowel is more difficult in an infant than in an adult. The diameter of the ureter of an infant is considerably less than the diameter of the ureter of an adult, and the muscularis layer of the rectosigmoid is thin. The

20. Higgins, C. C.: Transplantation of the Ureters into the Rectosigmoid in Infants: Review of Nineteen Cases, J. Urol. **50**:657-666 (Dec.) 1943.

serosal and muscularis layers must be incised with great care down to the mucosa, therefore, to form the trough in the intestinal wall to be occupied by the ureter. A modification of the Coffey technic is used. To prevent undue tension on the ureter with consequent kinking and angulation, the anastomosis must not be too tight. The operation in reality is a plastic procedure. It is Higgins' opinion that postoperative dilatation and hydronephrosis are due to technical errors and can be avoided.

Administration of ¼ to ½ fluidrachm (0.9 to 1.8 cc.) of camphorated tincture of opium U.S.P., according to age, is continued for one day after operation. The rectal tube inserted at operation is kept in place seven to ten days and may be irrigated gently at intervals to maintain its patency.

In this series of 19 cases of exstrophy of the bladder in which the ureters were transplanted into the rectosigmoid before the patient was 1 year of age, complications were negligible and the postoperative course was smoother than that for older children. In 1 case the wound disrupted on the sixth postoperative day. This complication is now avoided by using silver wire to close the abdomen. In 2 cases, after transplantation of one ureter into the rectosigmoid and cystectomy, nephroureterectomy was performed on the opposite side because of the presence of a large dilated ureter and infected hydronephrosis. The causative factor was obstruction at the ureterocystic junction.

Two of the infants died after operation.

Lower,[21] in discussing late results after transplantation of the ureters into the rectosigmoid, states that for the immediate future patients can be promised definitely that the risk of operation is greatly reduced, because the occurrence of peritonitis, which was rather common in earlier operations, is now practically eliminated. Until a sufficiently large series of cases has been followed over a long enough time, it cannot be stated what the social and economic status of the patient will be years later. Lower reports a series of cases which has been followed for more than twenty years. Out of 80 patients whose ureters were transplanted for conditions other than malignant lesions, 6 patients have survived for more than 20 years.

As Lower is now operating for this condition while the patient is still an infant, there is a relatively better chance of following these patients for a longer period than those on whom operation was performed when they were adults. Since 1932, when Lower first transplanted the ureters of a child 5 months old, he has advised the operation on infants.

He has included in this series of 80 cases only those in which operation was performed for exstrophy of the bladder, vesicovaginal fistula and Hunner ulcer, in other words, those cases in which urinary incontinence could not be corrected in any other way.

After trying out various technics, Lower has reduced the operation to the simplest possible form by using only absorbable ligatures and no mechanical aids whatsoever. There are certain points which should be emphasized. The first point, of course, is the careful preoperative preparation of the bowel. Adults receive a nonresidue liquid diet. One ounce (31 Gm.) of magnesium sulfate in 8 fluidounces (240 cc.) of water is given every morning daily in doses of 1 fluidounce (30 cc.) every fifteen minutes until the 8 fluidounces has been taken. The patient receives a daily cleansing enema. The day before operation no magnesium sulfate is given but cleansing enemas are ordered as frequently as necessary to clease the bowel completely of any fecal material. Ten minims (0.6 cc.) of tincture of opium is given three times on that day. The preoperative preparation should take between four and five days for complete emptying of the intestinal contents. In addition 1 Gm. of sulfasuxidine (succinylsulfathiazole) every four hours, four doses daily, for four days is given preoperatively. By this means, a double purpose is accomplished: first, a mechanical cleansing of the bowel and, second, an attempt at sterilization of the bowel.

If the patient is an infant, daily cleansing enemas are given but no magnesium sulfate is used. The diet consists of whole milk or milk formula, and no vegetables or cereals are allowed. The preoperative preparation lasts for three or four days. On the day preceding operation, dextrose water and water are substituted for the milk. Similarly, on the day before operation as many enemas are given as are necessary to obtain a clear return from the colon. On this day also from 1/4 to 1/2 fluidrachm (0.9 to 1.8 cc.) of camphorated tincture of opium U.S.P. is given three times, the dose depending on the age of the infant. Sulfasuxidine is given in amounts which also depend on the age and the weight of the child

Secondly, one must be especially careful to avoid angulation or constriction where the ureter is brought out from behind the peritoneum and is first attached to the bowel. In cases in which the ureter is transplanted for

21. Lower, W. E.: Late Results Following Transplantation of the Ureters into the Rectosigmoid, J. Urol. 50:581-584 (Nov.) 1943.

a shorter distance the patients seem to do better than in those cases in which the trough is too long and too much ureter is transplanted.

If the patient is an adult, unless there is a contraindication, Lower prefers to use spinal anesthesia, as it relaxes the abdominal muscles more completely than inhalation anesthesia, but if the patient is an infant he generally gives ether. In a number of cases both ureters have been transplanted at one procedure; this, he believes, is without any particular risk, especially for adults, unless there is some condition which might prolong the operation.

Of the series of 80 cases, data on 6 cases are presented in which the ureters were transplanted into the rectosigmoid more than twenty years ago; 3 patients are married, and none has been divorced. Their social and economic status has been restored.

Stevens and Lord [22] carried out a modification of the Coffey I technic of ureterointestinal anastomosis in the dog by means of a vitallium tube inserted into the end of the ureter. They draw the following conclusions:

> Suggestive evidence has been presented that the theoretical obstruction to urinary outflow caused by edema of the anastomosis is not the sole basis for the postoperative rise in the blood urea nitrogen. Improvement in the late results of ureterointestinal anastomosis of the Coffey I method by means of a vitallium tube was not obtained. Vitallium tubes in constant contact with urine and the bacterial flora of the sigmoid usually became calcified in 3-4 weeks.

Calculi.—Ainsworth-Davis [23] reports data on 20 cases of ureteral stone. He states that a large percentage of the smaller renal calculi, once they enter the ureter, will pass naturally without operative or instrumental intervention, though a number become impacted in either the upper or the lower portion of the canal. Those in the upper part should be removed by ureterolithotomy if they give rise to back pressure symptoms of renal pain or to signs of dilatation of the renal pelvis and calices, as shown by intravenous pyelography. When the stone, however, is held up in the lower part of the ureter, instrumentation should be given a trial before resort is made to operative measures. If the stone is actually in the intramural portion, it is usually a simple matter to insure its passage into the bladder within twenty-four to forty-eight hours by cutting the anterior ureteral wall overlying the calculus with a ureteral meatotome.

The patient is placed in the lithotomy position on a salt plate which is connected with one terminal of the diathermy machine. The cystoscope is passed, the obturator is withdrawn and the telescope, with a single catheterizing attachment and a meatotome, is inserted. After the latter has been connected to the other terminal of the diathermy machine, a survey of the bladder is made and the tip of the meatotome then is inserted into the obstructed ureter for a distance of 1.5 cm., great care being taken that the aperture of the diathermy knife is facing upward and inward, toward the cavity of the bladder. The knife is next made to present, by pressing the knob at the proximal end of the electrode, when a tentlike fold of anterior ureteral wall will be seen to be elevated, and with a touch of the foot switch the tip of the knife will emerge into the bladder. With the current on, gentle traction of the cystoscope will cause complete division of the wall of the ureter as far as its orifice, whereupon the knife is sheathed by pulling the knob of the meatotome, and the meatotome is withdrawn. When using the corkscrew maneuver, Ainsworth-Davis inserts the corkscrew past the stone by rotary motion and exerts traction. Traction can be continued for some time by means of a device of weights.

This method has been used on 20 patients. In all cases the stone was impacted in the lower part of the ureter. In most cases the stone was passed within several hours to three weeks after manipulation. In 1 case it was necessary to remove the stone by operation.

Wishard [24] states that three courses are open in the treatment of stones in the lower third of the ureter: 1. Spontaneous passage under observation is prudent in the face of progress if the stone is not too large, if the time required is not too long and if the patient is not suffering from too severe ureteral obstruction with its attendant stasis and infection. 2. Instrumental passage is safe if coincidental ureteral drainage and dilatation are maintained and if extraction is accomplished with flexible nonmetallic instruments. Instrumental passage should be abandoned in favor of surgical removal if progress ceases or if drainage becomes ineffectual and there is danger of attendant sepsis. The use of metallic extractors introduces hazards, which Wishard discusses. 3. Surgical removal should be used for stones which are disproportionately too large to pass or extract, or if it seems wise to abandon method 1 or 2. Surgical removal is safe and for the most part certain and free

22. Stevens, A. R., and Lord, J. W., Jr.: The Experimental Use of Vitallium Tubes in Ureterointestinal Anastomosis, J. Urol. **50**:574-579 (Nov.) 1943.

23. Ainsworth-Davis, J. C.: Calculi Impacted in the Lower Fourth of the Ureter: Their Removal by the Ureteric Corkscrew, Brit. J. Surg. **31**:34-38 (July) 1943.

24. Wishard, W. N., Jr.: Stone in the Lower Third of the Ureter with Report of an Instance of an Incarcerated Basket, J. Urol. **50**:775-783 (Dec.) 1943.

from the complications of method 2. In eighteen years Wishard has not had any deaths among private patients suffering from ureterolithiasis. An instance is reported illustrating failure with the extraction method, fracture of the basket and delivery of stone and basket from above.

Balkus [25] describes the use of a looped catheter in the treatment of ureteral calculi.

The materials required are a ureteral catheter, a strand of steel surgical suture wire (no. 33 or no. 35) approximately 6 inches (15 cm.) longer than twice the length of the catheter to be used and an ordinary pin. Since the catheter is employed usually in the attempt to extract stones from the pelvic segment of the ureter, it may be shortened to any desired length by removing a segment from its proximal end. This is desirable since less wire and effort are required to modify the shortened catheter. The latter should be whistle tipped and either no. 4 or no. 5 F., a no. 4 F. catheter being preferable, since it is easier to introduce and less likely to inflict injury.

With the exposed portion of the wire closely applied to the body of the modified catheter, the latter is passed into the ureter and to a point approximately 10 cm. beyond the level of the stone. Ureteral meatotomy has not been necessary in any of the cases, since the loop insures adequate dilatation. A small amount of liquid petrolatum is injected, after which the loop is formed by traction on the free end of the wire. The looped catheter then is withdrawn slowly. At the same time the ureteral orifice is kept under observation. As the stone held in the grasp of the loop enters the intramural segment of the ureter, bulging is noted, and at this time the beginning of the loop may be seen projecting through the ureteral orifice. The cystoscope may or may not be removed at this time. There is comparatively little danger of inflicting serious injury at this stage of the procedure, so that considerable traction may be applied. It is important to maintain the loop at all times. The calculus may appear firmly caught within the loop, as usually happens when the cystoscope has been removed prior to the final pull, or it may fall into the bladder as the loop is withdrawn. In some instances a second attempt is necessary, since the stone may slip out of the loop at a narrow meatus. An indwelling ureteral catheter is used for twenty-four to forty-eight hours after operation.

The success of the procedure depends primarily on introducing the modified catheter beyond the level of the stone. However, the loop provides an excellent means of dilating the ureter below the level of an impassable obstruction due to a stone and when it was so employed in 2 cases the stone subsequently came away spontaneously.

This technic has been employed successfully in 13 consecutive cases. In 3 of these a second attempt was necessary, since the calculus slipped out of the loop at the level of the ureteral orifice. The calculi in all of these cases occupied the pelvic segment of the ureter, the highest one having been arrested 9 cm. above the ureteral meatus.

Obstruction.—Deming [26] states that ureteropelvic obstruction due to extrinsic and intrinsic lesions of the ureter is a clinical entity and can be discussed as such by deleting all unknown and doubtful factors.

Causes of intrinsic obstruction at the ureteropelvic junction are thickening of the musculature, development of hyperplastic fibrous tissue and fibrous contracture which produces a small stoma. Causes of extrinsic obstruction are strands of fibrous tissue running across the ureter at the junction and aberrant vessels. Deming has selected for study only those cases in which the sole cause for obstruction was one of these and has deleted all those cases in which the obstruction may have been influenced by any other factor.

Deming's group numbers 82 cases, in each of which operation was performed. Thirty-five patients were male, and 47 were female. Thirty-seven had involvement of the right kidney and 29 of the left kidney. Sixteen had bilateral lesions. The greatest incidence of bilateral involvement is found in the second decade of life, but the largest percentage of infections is evident in the later decades. Thirty-five of the kidneys were infected. During the first two decades of life male patients were twice as frequent as female patients. After the twentieth year, female patients predominated. During the first two decades of life, the left kidney was more frequently involved than the right kidney. This is in accord with the general opinion that congenital abnormalities of the urinary tract are more common on the left than on the right side.

During the first two decades of life, the extrinsic and intrinsic lesions were distributed about equally. In the third decade, in 9 cases there was definite thickening of the junction and in 1 there was contraction. Aberrant vessels

25. Balkus, V. A.: A Looped Catheter in the Treatment of Ureteral Calculi, J. Urol. **50**:667-672 (Dec.) 1943.

26. Deming, C. L.: Ureteropelvic Obstruction Due to Extrinsic and Intrinsic Lesions of the Ureter as a Clinical Entity and Its Treatment, J. Urol. **50**:420-431 (Oct.) 1943.

were common, and it was not at all clear in some cases in which there were both bands of fibrous tissue and vessels whether the vessels or the adhesive bands of fibrous tissue were the primary factor. In the fourth and fifth decades of life distribution of extrinsic and intrinsic lesions was about equal. In the seventh decade there were only 2 cases, in both of which the lesion was intrinsic. The total number of intrinsic lesions was 37, while the total number of extrinsic lesions was 50, 24 of which were due to bands of fibrous tissue and 26 to vessels. There is no doubt that there is a congenital factor which plays a large part in the early decades of life. Aberrant vessels are, of course, congenital.

The object of plastic procedures should be maintained: (1) to produce a physiologic emptying of the renal pelvis by one plastic operation or a combination of plastic operations and (2) to preserve the renal function by maneuvering the kidney into a position favorable for preservation of the physiologic function of the pelvis and by conserving all aberrant vessels. The surgical procedures can be classified roughly as (1) nephrectomy, (2) plastic procedures on the renal pelvis, (3) plastic procedures on the ureter, (4) combined plastic procedures on the pelvis and the ureter and (5) nephropexy. Some patients were treated with a combination of these operations.

Nephrectomy was done only when it seemed essential, as in cases in which the cortical substance of the kidney had been destroyed completely. In this series nephrectomy was done in 40 cases (about 48 per cent). In every case the kidney belonged to the completely nonfunctioning group. Nephrectomy was common in the first decade and in the later decades of life; it was least common in the adolescent period. Nephrectomy was done in only 3 of the 16 cases in which the lesions were bilateral. The remainder of the 40 cases in which nephrectomy was done were those in which there had been a relatively long duration of symptoms, which caused complete destruction of the cortical portion of the kidney.

Twenty-seven patients were treated by various plastic procedures on the pelvis and on the ureters, 10 by ureteropyeloplasty, 7 by reimplantation of the ureter, 3 by the Rammstedt operation and 2 by Y-plasty. Resection of the redundant pelvis, which was done in 13 cases, was distributed more or less throughout the decades of life but was used only once on a patient in the first decade of life.

In 15 of the 42 kidneys conserved, the ureteropelvic obstruction was corrected by lysis of the kidney and the upper part of the ureter and nephropexy. Nephropexy was most commonly used for patients in the second decade of life. In many cases nephropexy was done in conjunction with plastic procedures.

In the 15 cases in which treatment was by lysis and nephropexy alone, all the patients were relieved successfully of their symptoms and renal function was preserved. Ten of the 27 patients on whom the various plastic measures were used had supplementary nephropexy. In 2 of the cases of plastic procedure the result must be considered unsuccessful because subsequent nephrectomy was required. Both of the patients had ureteropyeloplasty of the Finney type.

Two of the patients treated by the Rammstedt operation leaked urine for one and two days respectively, but the urine did not become infected, and the patients were entirely relieved of their symptoms. The postoperative retrograde cystoscopic studies in these cases show that the pelves empty and that the physiologic function of the kidneys is maintained. Patients who had reimplantation of the ureter into the dependent portion of the pelvis did well. For suture material no. 00000 chromic catgut was used as individual sutures, reenforced with a layer of fascia. Urinary antiseptics were used in all cases, both therapeutically and prophylactically. Since the advent of sulfonamide compounds, drainage has not been used in the plastic procedures except in those cases in which infection existed at the time of operation.

The results of Deming's experience with patients suffering from obstruction of the ureteropelvic junction are as follows: There have not been any operative deaths. Nearly all types of plastic procedures have been tried, and there have been only 2 cases in which plastic procedures were unsuccessful. All other patients were entirely relieved of their symptoms, and the kidneys functioned well. Nephrectomy was done in 3 cases of bilateral ureteropelvic obstruction in which hydronephrosis was complete, without any function in the kidney which was removed. In a relatively large number of cases nephrectomy was done when there was unilateral nonfunctioning hydronephrosis, which indicated in most cases long periods of obstruction.

Kidneys which are infected require drainage when plastic operations are done. For the last few years the gallbladder T tube has given satisfactory results. A no. 12 to no. 14 F. tube is inserted into the normal ureter through a small longitudinal incision about 4 cm. below the field of plastic repair, with the lower arm extending downward 1 cm. and the longer arm extending

upward well into the pelvis of the kidney. Two or three extra holes are cut into this arm to provide adequate drainage. By this method the surgeon can avoid a nephrostomy incision. The method also offers an opportunity to irrigate the pelvis and, by closing the tube, to induce normal flow of urine down the ureter. This tube is left in place ten to fourteen days and then can be removed readily. By the end of this time a sufficient walled-off fistulous tract is produced so that one would not anticipate any difficulty of healing of these wounds. No untoward accidents have happened, nor have there been any draining ureteral fistulas. Some ureters leak a little urine for a day or so, but the majority do not drain any urine.

From experience with these cases of extrinsic and intrinsic ureteropelvic obstruction, Deming concludes: Fundamental surgical principles for plastic procedures in general can be applied in the correction of obstruction of the ureteropelvic junction. No one plastic procedure is adequate for the correction of all types of ureteropelvic obstruction. Lysis with nephropexy is adequate in many cases. The Rammstedt technic should be applied more frequently than it is and should be accompanied by fixation of the kidney. Conservation of the aberrant blood vessels is essential. All infected kidneys must have drainage after plastic procedures. Infection of the kidney clears more rapidly after ureteral reimplantation than after ureteropyeloplasty. Chemotherapy is a great adjunct to plastic surgery of the renal pelvis. However, the surgeon should not sacrifice good technic because of the use of the sulfonamide compounds. Since diagnosis of ureteropelvic obstruction is possible when the patient is an infant or a child and the various plastic procedures can be used successfully, the number of cases in which nephrectomy is performed should be reduced. Uninfected hydronephrotic kidneys that have impaired function due to ureteropelvic obstruction should not be harmed at the time of plastic procedures by infection produced with the use of drainage tubes and splints.

Ureterocele.—Emmett and Logan [27] report data on a case of ureterocele with prolapse through the urethra. The patient was a girl aged 2 years who since infancy had had urinary frequency, incontinence and dysuria. The urine contained pus, and the excretory urogram revealed some dilatation of the right ureter and kidney and a large filling defect in the bladder. At cystoscopy a large mass was encountered lying in the base of the bladder. The mass could be moved from side to side and was attached to the right side of the base of the bladder. Several cuts were made in this tumor mass with the Bugbee electrode, but there was no distinct collapse of the mass, such as is usually seen in the ordinary case of ureterocele. By means of the no. 18 F. Thompson infant resectoscope the mass was removed completely. Afterward the child voided normally, and all her urinary symptoms disappeared.

In a review of the literature, it was found that data on more than 37 similar cases had been reported. In 37 cases reported the patients were female. Twelve were children who ranged in age from 13 days to 14 years. Only 5 of the 12 children survived operation. The first patient reported in the literature who had a prolapsed ureterocele and who survived an operation was a girl 14 years of age. Two of the older patients, who were between 20 and 30 years of age, had had prolapses of their ureteroceles when they were younger, 1 when she was only 8 years of age.

The cause and the pathogenesis of ureterocele have been discussed widely. The consensus seems to favor a congenital origin. As a result of congenital stenosis of the ureter, which also may be due sometimes to an inflammatory condition, and probable congenital weakness of the wall of the lower part of the ureter, dilation of this part of the ureter takes place and then ballooning out into the bladder occurs. Prolapse occurs when the lesion becomes large. The size and the appearance of the prolapsed ureterocele have been compared to those of a ripe fig or a tomato. Ureteroceles are lined on their vesical aspect by vesical mucosa and internally by ureteral mucosa, between which are fibrous tissue and some smooth muscle fibers.

Prolapse of the ureterocele through the urethra is accompanied by pain, dysuria and bleeding. Anuria occurs if the tumor blocks the urethral opening completely. Frequently the diagnosis can be made on seeing the lesion, providing that the physician is aware of the possibility of occurrence of the condition. The diagnosis can be confirmed by excretory urography and cystoscopic examination.

In most of the cases reported in recent years in which an accurate preoperative diagnosis has been made, open surgical methods of treatment have been employed. The most common procedure is to open the bladder suprapubically and excise the protruding ureterocele. Most uretero-

27. Emmett, J. L., and Logan, G. B.: Ureterocele with Prolapse Through the Urethra, J. Urol. **51**:19-23 (Jan.) 1944.

celes can now be cared for transurethrally. In the average case simple excision of the ureterocele with the cutting diathermy current will prove sufficient, as the collapsed sac left behind will atrophy or slough away. In the occasional case, however, as in the one reported by Emmett and Logan, the walls of the sac may become so thickened from inflammation, trauma and edema that it is of sufficient bulk to act as a foreign body of more or less solid consistency. In such a case complete removal of the sac with the resectoscope will be necessary.